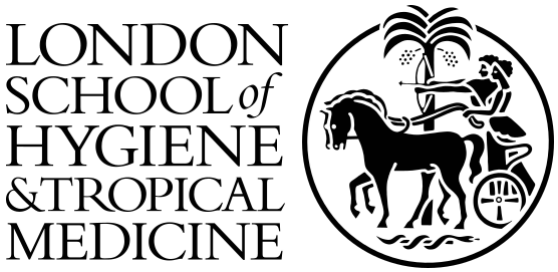

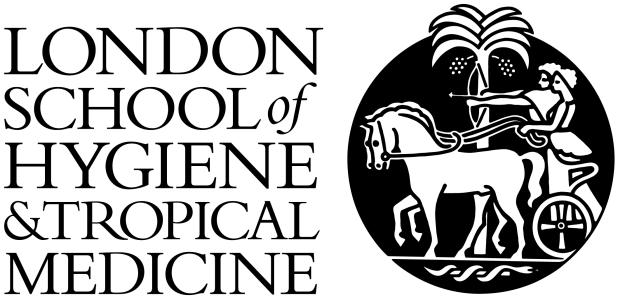

The Nakuru Eye Disease Cohort Study

Andrew Bastawrous

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Prof. Hannah Kuper [primary supervisor]

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Abstract

Objective: To provide six-year cumulative incidence of visual impairment and blindness, diabetic retinopathy (DR), age related macular degeneration (AMD), visually impairing cataract and features of glaucoma in an older age Kenyan population and the risk factors for each.

Design: Population based cohort study with six-year follow-up (n=2,171; 50% participation)

Main outcome measures: Six-year cumulative incidence of visual impairment and blindness, DM, DR, AMD, visually impairing cataract and features of glaucoma, risk factors for incidence and population estimates.

Results: The six-year cumulative incidence of visual impairment and blindness was 119.4 (103.1 - 137.9) and 15.1 (10.4 – 21.7) per 1000 of population respectively. The six-year cumulative incidence of DM and DR (in those with diabetes mellitus) was 61.0 (50.3 - 73.7) and 224.7 (116.9 - 388.2) per 1000 of population respectively. The six-year cumulative incidence of AMD was 164.2 (136.7 - 195.9) per 1000 of population and the six-year cumulative incidence of visually impairing cataract was 235.6 (213.5 – 259.3) per 1000 of population. Associations with incident cases were demonstrated for each with age and diabetes being the leading associations across the primary outcome measures.

Conclusions: This six-year follow-up of a population-based cohort indicates a high incidence of visual impairment and blindness and provides data, for the first time, on the incidence of DR, AMD and cataract in Kenya. A large gap exists between provision and need for services and cataract control should remain the priority focus with work to strengthen health care systems as posterior segment eye diseases will become a greater issue as services improve and cataract comes under greater control.

Abbreviations:

AMD	Age-Related Macular Degeneration
AREDS	Age Related Eye Diseases Study
BDES	Beaver Dam Eye Study
BMES	Blue Mountain Eye Study
CBM	Christoffel Blinden Mission
CI	Confidence Interval
CO	Corneal Opacity
CNVM	Choroidal Neovascular Membrane
CSME	Clinically significant macula (o)edema
D	Dioptres
DALYs	Disability-adjusted life years
DEFF	Design Effect
DM	Diabetes Mellitus
DR	Diabetic Retinopathy
ET	Examination Team
ETDRS	Early Treatment of Diabetic Retinopathy Study
FDT	Frequency Doubling Technology
GA	Geographic Atrophy
GAT	Goldmann Applanation Tonometry
HIV	Human Immunodeficiency Virus
IAPB	International Agency for the Prevention of Blindness
ID	Identification
IOP	Intraocular pressure
IOVs	Inter observer variations
IRMA	Intraretinal Microvascular Anomalies
ISGEO	International Society Geographical & Epidemiological Ophthalmology
LALES	Los Angeles Latino Eye Study
LMIC	Low and Middle Income Countries
mmHg	Millimeters of mercury
NCDs	Non-communicable Diseases
NPDR	Non-Proliferative Diabetic Retinopathy
OCO	Ophthalmic Clinical Officer
PDR	Proliferative Diabetic Retinopathy
POAG	Primary Open Angle Glaucoma
PSED	Posterior Segment Eye Disease
PY	Person-years
RAAB	Rapid Assessment of Avoidable Blindness
RVPGH	Rift Valley Provincial General Hospital
SSA	Sub-Saharan Africa
TBC	To be confirmed
USA	United States of America
VA	Visual Acuity
VCDR	Vertical Cup to Disc Ratio
VF	Visual Fields
VI	Visual Impairment
WHO	World Health Organisation

Format of the Thesis

The thesis for this PhD is in the "research papers" format and includes a number of published papers (7) as well as two being submitted for peer-review and publication.

Chapters listed in italics in the Contents are in this research/review paper format, and includes publication details in a cover sheet, including acknowledgement of contributions.

The other chapters of the thesis are composed of "linking material" which includes information/data not covered in the research papers and helps to make the thesis a coherent body.

CONTENTS

Acknowledgements

This work is dedicated to Madeleine, my wife and best friend. Thank you for stepping into and embracing the unknown with me.

Thank you. x

Special thanks to my supervisors, Professors Hannah Kuper and Matthew Burton who's skill sets, mentoring and continued support throughout could not have been better. I struck gold. It has been an absolute pleasure to learn from you and I'm so pleased to be able to continue to work alongside you.

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To all the many friends, family and colleagues who have been with me through out, especially my beautiful two children, Lucas and Elena, the first who grew up in Kenya and the second who was made in Kenya. I suspect you'll never read this thesis but I hope you have seen and experienced things that are recorded here that will stay with you for life.

And finally, to the millions in the world who remain needlessly blind, all of this is ultimately for you, I hope in some small way this work contributes to you being heard.

Chapter 1. Introduction

This chapter will provide an overview of eye disease in sub-Saharan Africa (SSA), what we know, and gaps in knowledge that this thesis hopes to contribute to filling. Cataract and Posterior Segment Eye Disease (PSED) in SSA will be reviewed in more detail in chapters 2 and 3.

In recent decades there has been a marked rise in life expectancy that has contributed to a major epidemiological shift in populations worldwide. (1) These changes have led to the emergence of new major public health issues in low and middle-income countries (LMIC). (2) Current projections suggest that non-communicable diseases (NCDs), such as diabetes mellitus and hypertension will contribute to two-thirds of global mortality by the year 2030. (2) The emergence of NCDs in LMICs, including in SSA is happening at an alarming rate with the Global Burden of Disease study showing that the leading cause of death in people from Africa aged 60 years and over is already NCDs. (3) NCDs in LMIC have shown substantial variation in prevalence, incidence, natural history and risk factors to NCDs in populations in high-income countries and so a detailed local understanding is needed for us to effectively respond to this growing public health problem.

The majority of existing data on NCDs from LMIC are from cross-sectional studies providing valuable data on prevalence and risk factors. Longitudinal studies provide the opportunity to investigate the natural history of diseases, which is necessary in developing health policies at local and national levels. Longitudinal cohort studies from LMIC are few due to barriers including: expense; complex logistical planning; and political challenges. Inferring data from high-income countries is inappropriate due to the unique combination of genetic and environmental factors in other

contexts, and moreover undermines efforts to establish studies in LMIC which will guide the effective use of minimal existing resources to deal with the growing burden of NCDs.

As the disease profile is changing from infectious (communicable diseases) to NCDs in LMICs, this is also happening for the causes of blindness. 285 million people are visually impaired (VI) worldwide, of whom 39 million are blind. (4) Approximately 90% of those worldwide with VI live in low-income countries. NCDs (e.g. cataract, refractive error) are the leading causes of VI, in part due to the successful control of infectious causes of VI such as trachoma and onchocerciasis.(5-7) VI is ranked sixth in the top ten causes of burden of disease in terms of disability-adjusted life-years (DALYs) worldwide in the Global Burden of Disease Study. (8)

The number of people visually impaired in the World Health Organisation (WHO) African region is estimated to be 26 million of whom, almost 6 million are blind. (4) Despite Africa having a high prevalence of blindness, it is the most underserved continent in terms or human resources available to treat and manage eye disease, (9) with the greatest gap between existing need and provision. (10)

The Global Burden of Disease Study conducted a major review of the prevalence of blindness in SSA and trends over two decades (1990-2010). Overall the prevalence of blindness and VI had reduced although the absolute number of people who are blind or VI had gone up in this period. In 2010 the estimated age-standardised prevalence of blindness was 1.3% (95% CI 1.1% to 1.5%) and visual impairment was 4.0% (95% CI 0.2% to 0.3%). The major causes of blindness were; cataract 35%, other/unidentified causes 33.1%, refractive error 13.2%, macular degeneration 6.3%,

trachoma 5.2%, glaucoma 4.4% and diabetic retinopathy 2.8%. (11) PSED are defined as conditions primarily affecting the back of the eye include Diabetic Retinopathy, Age-Related Macula Degeneration, and Glaucoma.

Cross-sectional population based studies from the last two decades performed in SSA support the main rends reported from the GBD. While cataract often dominates as the cause of blindness, these surveys have shown glaucoma and/or PSED to be either the primary or secondary cause of blindness in multiple countries. This includes studies from Kenya, (12, 13) Nigeria, (14) Tanzania (15), Rwanda (16), Cameroon (17), Ghana (18), Zanzibar (19) and Guinea (20).

Posterior segment eye diseases (PSED) differ from the leading anterior segment eye diseases (cataract and refractive error) in prevention/treatment, as no cures currently exist (with the exception of angle closure glaucoma). Surgical intervention can restore vision in those visually impaired from cataract and provision of glasses can restore or improve vision in people with refractive error. However, those who have established visual loss from PSED cannot be cured (See Figure 1). Medical and/or surgical intervention for glaucoma can slow disease progression and thereby prevent sight loss. (21) Systematic control of diabetes mellitus (DM) and laser treatment to the retina in sight-threatening DR can stabilise and, to a small degree, improve DR status and thereby also prevent sight loss. (22) Currently no known cure for AMD exists, although intravitreal therapy is available for end-stage wet AMD (approximately 10% of all AMD cases). It is currently prohibitively expensive for use in most LMIC, but is widely used in high-income countries. (23) Vitamin supplementation has shown some evidence of risk reduction of progression of

subtypes of AMD (24) but not prevention of AMD (25), but again may be prohibitively expensive. It is therefore imperative that PSED are diagnosed early in their course so that early treatment and prevention of vision loss can be a realistic target. This remains true in SSA, as well as in other world regions.

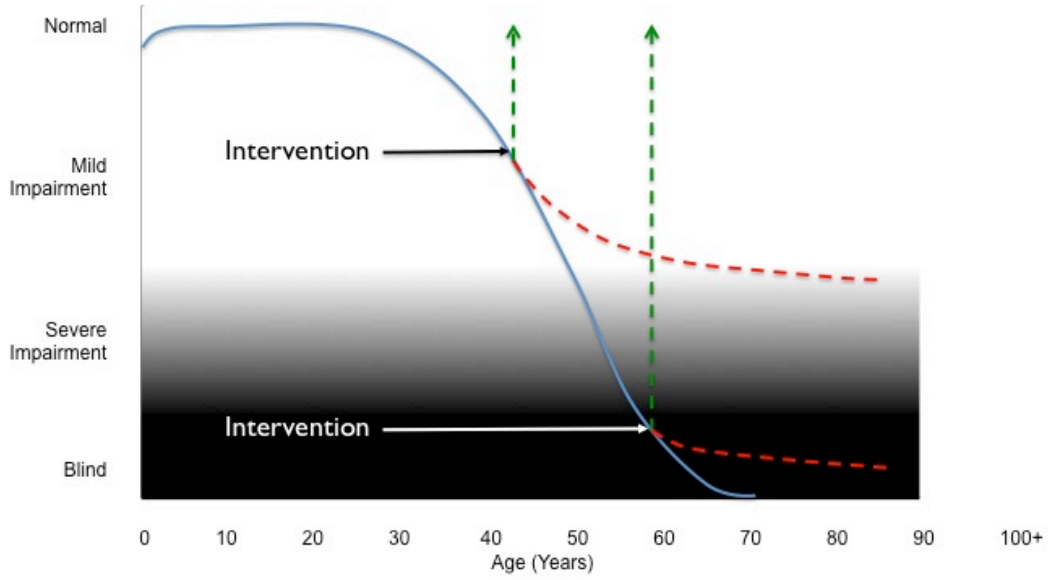

Figure 1. Blue curve showing progressive sight loss with age. Green dotted line shows effect of intervention in anterior segment disease (cataract, refractive error), i.e. sight restoration. The red dotted line shows the effect of intervention with PSED, i.e. Reduction in rate of visual loss.

Although PSED are frequently collated and presented as a single condition or group of conditions, they are clinically and pathophysiological distinct. The most common types of PSED are Diabetic Retinopathy, Age-Related Macula Degeneration, Glaucoma. These conditions form the focus of this thesis, and are described here briefly.

Glaucoma is a group of eye diseases leading to progressive sight loss. The common feature of glaucoma is damage to the optic nerve, which results in progressive loss of visual field until eventually the central vision is affected. (26) Glaucoma can be sub-divided anatomically based on the angle formed between the cornea and iris. Primary open-angle glaucoma (POAG) is more common in African and Caucasian populations and Narrow-angle glaucoma more common in Asian populations. The only known modifiable risk factor is intraocular pressure (IOP), which can be reduced through topical, oral or intravenous medication, laser procedures or surgery.

Diabetic retinopathy (DR) is one of the micro-vascular complications of diabetes and is a severe ocular complication of diabetes. DR is defined as the presence of typical retinal microvascular signs in an individual with diabetes mellitus (DM). Hyperglycamia (elevated blood sugar) initiates several vascular events (see figure 2)

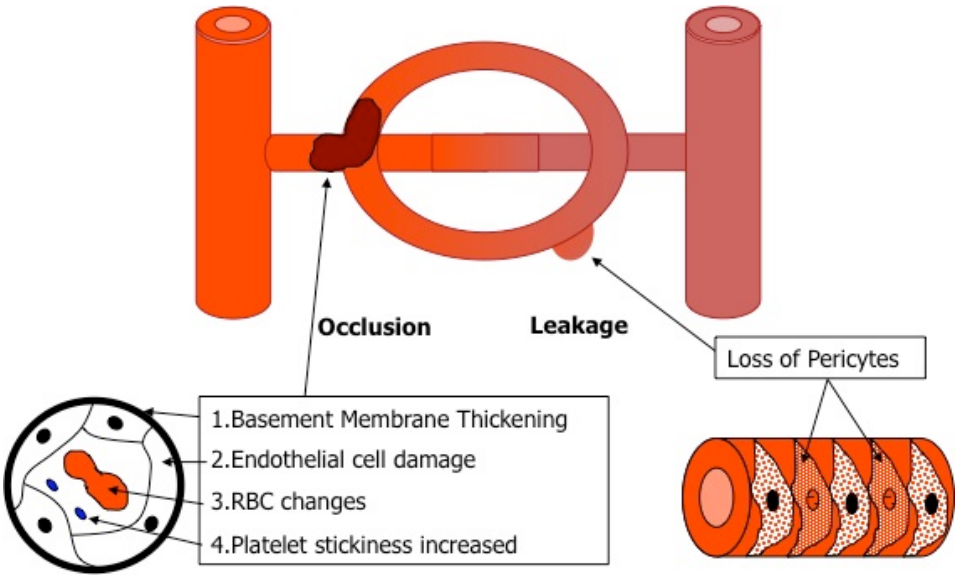

Figure 2. Pathogenesis of Diabetic Retinopathy

Vision loss develops from the sequelae of these pathophysiological changes at the macula, known as maculopathy (macular oedema and ischaemia) and from the formation of fragile new blood vessels known as proliferative disease. Proliferative DR can lead to vitreous haemorrhage and retinal detachment. (27)

These processes lead a variety of the clinical manifestations. DR is graded on the basis of these features:

- Microaneurysms
    - outpouchings in the vessel walls due to pericyte loss
- Retinal haemorrhages
    - leakage of blood from blood vessels in to the retina
- Infarcts of the retinal nerve fibre layer known as 'cotton wool spots'
    - due to local ischaemia from poor blood/oxygen supply
- Intra-retinal microvascular abnormalities (IRMA)
- Venous vessel wall dilatation ('beading')
- Neovascularisation (new-vessel formation), seen on the disc, retina or iris

Good control of blood sugar and blood pressure by persons with diabetes reduces the risk of developing DR, however prevention of diabetes in the fist plae must remain the primary public health concern.

AMD is a degenerative condition affecting the central retina leading to central vision loss. It is highly associated with age and multiple classification systems are in use. (28)

Common descriptive terms include "dry" and "wet" AMD and "early" and "late" or "advanced" AMD. Most vision loss occurs in the late stage of the disease, which is defined as the presence of atrophy or neovascularisation. In the dry form of the disease, deposits known as drusen are deposited between the retina and choroid and subtypes of drusen (based on size and morphology) form part of the more detailed classifications. Wet AMD leads to destruction of the macula architecture due to abnormal vessel growth (neovascularisation). These new vessels break through Bruch's membrane from the choriocapillaris. Leakage (blood and protein) from new vessels leads to photoreceptor damage and ultimately sight loss.

Posterior Segment Eye Disease in Africa

Cross-sectional population based studies from the last two decades performed in SSA have shown glaucoma and/or PSED to be either the primary or secondary cause of blindness. This includes studies from Kenya, (12, 13) Nigeria, (14) Tanzania (15), Rwanda (16), Cameroon (17), Ghana (18), Zanzibar (19) and Guinea (20) (See table 1). No longitudinal data on PSED from population-based studies in Africa have been published. A single cohort in Uganda has three-year cumulative incidence data on visual impairment, (age standardised incidence rate of 13.2, per 1000 PY) with AMD and glaucoma amongst the leading causes of visual loss in new cases. (29) However, no baseline data of eye health status was available in the incident cases.

The majority of available prevalence data in SSA comes from the Rapid Assessment of Avoidable Blindness (RAAB) methodology (31), which, although a validated survey method (13), like more comprehensive surveys such as the Nigeria study (32) only examine eye health status in those found to have existing visual impairment. Since glaucoma patients only lose central vision at the end stage of the disease they are frequently missed unless visual field assessment is performed.

Table. Primary and secondary causes of blindness and visual impairment by country in which a population based study has been performed

Country	Main cause of blindness	2nd Main cause of blindness	Main cause of VI	2nd Main cause of VI
Nigeria	Cataract (43.0%)	Glaucoma (16.7%)	Refractive Error (57.1%)	Cataract (25.8%)
Tanzania	Cataract (51.2%)	PSED (35.7%)	Cataract (54.8%)	Refractive Error (32.7%)
Kenya	Cataract (42.0%)	PSED (30.4%)	Cataract (36.0%)	Refractive Error (31.5%)
Rwanda	Cataract (65.0%)	PSED (20.0%)	Cataract (54.7%)	Refractive Error (29.9%)
Eritrea	Cataract (55.1%)	Glaucoma (15.2%)	Cataract (55.4%)	Refractive Error (30.9%)
South Sudan	Cataract (41.2%)	Trachoma (35.3%)	Trachoma (58.1%)	Cataract (29.3%)
Cameroon	Cataract (62.1%)	PSED & Oncho (13.8%)	Cataract (40.0%)	PSED (27.8%)
Cameroon	PSED (29%)	Cataract (21%)	Cataract (48%)	Refractive Error (22%)
Zanzibar	Cataract (67%)	PSED (25%)	Cataract (47%)	Refractive Error (39%)
Ethiopia	Cataract (49.9%)	Trachoma (7.7%)	Cataract (42.3%)	Refractive Error (33.4%)
Ethiopia	Cataract (50.4%)	Trachoma (19.5%)	Cataract (33.7%)	Refractive Error (25.5%)
Guinea	Cataract (61.3%)	Macular affection (25.3%)	Cataracts (86.6%)	Macular affection (29.3%)
Malawi	Cataract (48.2%)	Glaucoma (15.8%)	Cataract (46.3)	Refractive Error (41.1%)
Uganda	Glaucoma (38.5%)	Cataract (23.1%)	Cataract (57.4%)	Refractive Error (18.5%)
Nigeria	Cataract (46%)	Surgical complications (20%)	Cataract (40.3%)	Refractive Error (39.8%)

The majority of these surveys have used the WHO coding instructions, which use the "principal" disorder responsible for visual loss in the individual after considering disorders in either eye which are most amenable to treatment or prevention"(30). In other words, if a patient has PSED co-existent with cataract it will be deemed that cataract is the primary cause of blindness/VI. Therefore most VI prevalence data available in which cataract or refractive error is the primary cause will underestimate the prevalence of PSED.

Glaucoma in Africa

Current estimates suggest that there are 6.5 million people with glaucoma in sub-Saharan Africa (SSA) with a projected increase to 8.4 million in 2020 (33). Glaucoma is estimated to be the second leading cause of blindness in Africa (34). These estimates are based on only seven population-based studies, of which two examined individuals of Africans descent living outside of the African continent: in Baltimore, USA (35) and Barbados (36). Of the five based in Africa, three were undertaken in South Africa (37-39) one in Ghana (40) and one in Tanzania (41). The studies used varying sampling methods and criteria for diagnosis of glaucoma.

No specific and sensitive test for glaucoma exists. Current gold-standard diagnosis requires expensive visual field-testing equipment with expert interpretation of optic disc changes and visual field findings; the diagnosis is relatively subjective with poor agreement between experts. (42) Standardised definitions and classifications of glaucoma in recent years have allowed for better prevalence estimates and comparisons between populations. (26)

There are several unique characteristics of glaucoma in Africa. First, POAG disproportionately affects individuals of African descent (33). This condition is difficult to diagnose in early disease and when diagnosis is confirmed there is still debate on the best management in the context of limited resources and prospects for long-term follow up (43). Second, studies have shown that those of African descent (not living in Africa) have a higher prevalence of glaucoma, are more likely to develop glaucoma at an early age with more aggressive diseases and a higher risk of

glaucoma related blindness than Caucasians or Asians. (44, 45). It is therefore vital that the epidemiology of glaucoma is investigated in more detail in various populations in Africa. This includes investigation of the progression and incidence of glaucoma in Africa, as this data is currently lacking.

Diabetic Retinopathy in Africa

Diabetes is a major threat to global public health. The estimated prevalence of diabetes worldwide was 285 million in 2010, representing 6.4% of the world's adult population, with a prediction that by 2030 there will be 438 million people with diabetes (46). The most substantial increases (7 to 15 million, 111%) between 2010 and 2030 are expected to be in Africa and the Middle East as a result of population growth, ageing, and the increase in obesity and sedentary lifestyles in these regions (47). The predicted rise in proportion of adults suffering from diabetes will inevitably lead to an increase in the prevalence of DR (48).

The detection of DR in Africa remains a challenge; a lack of necessary equipment and skilled human resources (49) has contributed to there being minimal evidence available of the contribution of DR to blindness in African countries.

Studies investigating DR in Africa have been reported in Egypt, (50) Mauritius, (51) South Africa (52) and Nigeria. (14) These studies are not generalisable to other countries in Africa, since populations in Egypt and Mauritius are ethnically and demographically different to the majority of African populations, the study in South

Africa examined only Indian sub-population and the study in Nigeria only assessed DR in those with existing VI.

Africa is on the cusp of a DR epidemic and data are urgently needed on the incidence and progression of DR in order to plan treatment and preventive services. More information is also needed on predictors of DR in Africa, as these may vary compared with other settings. For instance, retinopathy may occur early in the course of diabetes in Africa because of late diagnosis, inadequate control of diabetes, and co-occurring hypertension, (53) and possibly progression is more rapid in populations of African origin (54).

Age-Related Macular Degeneration in Africa

The majority of data globally on AMD are from Caucasians and Asian populations (55-63) with a paucity of data from people of African descent. Data that do exist are largely from studies undertaken in African populations living outside of the African continent.(64, 65). Comparative data between Caucasians and Africans living in the same geographical area have suggested differing predispositions towards AMD, with possible genetically protective factors for AMD progression in individuals of African descent compared to their Caucasian counterparts (Baltimore, USA).(66) Population-based evidence of African populations living in Africa on the prevalence, incidence and progression of the disease, and of the risk factors for AMD is currently absent, but important to collect in order to plan services and gain a better

understanding of the aetiology of the disease. Despite recent data it is still a widely held belief that the prevalence of AMD in Africa is low.

Eye care services in Africa

VISION2020 is the global initiative for the elimination of avoidable blindness, launched in 1999, jointly by the WHO and the International Agency for the Prevention of Blindness (IAPB) and provides technical support and advocacy to prevention of blindness activities worldwide. It aims over two decades to prevent 100 million people from becoming blind. *(67)* The focus of IAPB has been on cataract and refractive error, as leading causes of VI, as well as on causes important to eliminate such as trachoma and onchocerciasis. As these conditions are being brought under control it will be important for IAPB to develop strategies for the control of PSED, which will require the generation of more robust data on these conditions from SSA where the prevalence of blindness is highest in the world.

There is wide variability between eye health service availability in different countries and within countries in SSA. The WHO has established targets on the number of eye care providers needed per million of population based on the knowledge that 75% of vision loss is due to a combination of uncorrected refractive errors and cataract. (68) However, very few countries in SSA currently meet the VISION2020 human resource target (five in total) for number of ophthalmologists/cataract surgeons and no country has yet made the target number of optometrists/refractionists. (69) Kenya, the focus country of this study, has met the target for ophthalmologists, but it remains, however, well below the target cataract surgical rate of 2,000 surgeries

per million of population per year (only the Gambia and Sudan are on target).The chronic nature of PSED and complexities in their control, makes this a pressing issue in terms of supporting under resourced health systems and establishing evidence based estimates for both the magnitude and incidence of diseases that are growing in public health significance.

The focus of this thesis is therefore to explore the incidence and progression of PSED, in order to gain a deeper understanding of the aetiology of these conditions, and to generate data for planning of eye care services in SSA.

Research and thesis overview

The review chapters assess the current epidemiological understanding of both cataract (chapter 2) and posterior-segment eye diseases (chapter 3) in sub-Saharan Africa from population based cross sectional studies and the regional specific data which forms the baseline of this cohort. (chapter 4) is a summary of the baseline findings from the cohort and the rationale for follow-up. (chapter 5) looks at the relationship of ophthalmic human resources and the prevalence of blindness globally and the gap between need and provision in sub-Saharan Africa.

The methods detailing how the study was undertaken are described in (chapter 6).

The data chapters provide the incidence of blindness and visual impairment (chapter 7), diabetes mellitus and diabetic retinopathy (chapter 8), age related macula degeneration (chapter 9), features of glaucoma in the population (chapter 10) and the incidence of cataract (chapter 11).

The discussion section includes a summary of the results (chapter 12), and how the results fit in to the broader context, strengths and limitations of the study, ongoing and future research and new methods (Peek) for collecting population based survey data and delivering screening programmes.

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Chapter 2. Blindness and visual impairment due to age-related cataract in sub-Saharan Africa

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Student	Andrew Bastawrous
Principal Supervisor	Hannah Kuper
Thesis Title	The Nakuru Eye Disease Cohort Study

If the Research Paper has previously been published please complete Section B, if not please move to Section C

SECTION B – Paper already published

Where was the work published?	British Journal of Ophthalmology		
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Blindness and visual impairment due to age-related cataract in sub-Saharan Africa: a systematic review of recent population-based studies

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ABSTRACT

Aim We aimed to evaluate age-related cataract as a contributor to blindness and visual impairment (VI) in sub-Saharan Africa (SSA).

Methods A systematic review of population-based studies published between 2000 and October 2012. Prevalence and proportions of blindness and VI due to cataract, cataract surgical coverage (CSC), per cent intraocular lens (IOL) implantation and visual outcomes of surgery in accordance with WHO criteria were ascertained.

Results Data from 17 surveys (subjects mostly aged ≥50-years-old) from 15 different countries in SSA were included, comprising 96 402 people. Prevalence of blindness (presenting visual acuity <3/60 in better eye) ranged from 0.1% in Uganda to 9.0% in Eritrea, and the proportion of total blindness due to cataract ranged between 21% and 67%. Cataract was the principal cause of blindness and VI in 15 and 14 studies, respectively. There was a strong positive correlation between good visual outcomes and IOL use (R=0.69, p=0.027). Considerable inter-study heterogeneity was evident in CSC and visual outcomes following surgery, and between 40% and 100% of operations had used IOL.

Conclusions Cataract represents the principal cause of blindness and VI and should remain a priority objective for eye care in SSA. However, the prevalence of blindness and VI due to cataract was variable and may reflect differences in the availability of cataract surgical programmes and cataract incidence.

INTRODUCTION

Cataract can manifest across one's lifespan but its prevalence and incidence rise with increasing age. Age-related (or senile) cataract is the most common cause of cataract in adults. The burden of cataract is expected to continue to pose a greater challenge to healthcare systems worldwide in future years, consistent with population ageing and increases in life expectancy.[1] Of 39 million people estimated to be blind worldwide in 2010, 51% of cases were attributed to cataract.[2] Regional variations in the prevalence and incidence of blindness and visual impairment (VI) due to age-related cataract exist, with a disproportionate prevalence in low- and middle-income populations. Africa is home to 11.9% of the global population, but 15% of the world's blind, the majority of which is due to cataract.[2]

As no effective prevention strategies exist, management of cataract is principally surgical removal of the lens with simultaneous correction of aphakia. In SSA, extra-capsular cataract extraction is usually now performed, increasingly using a small-incision approach, although the use of phacoemulsification is rising. Cataract surgery constitutes one of the most cost-effective of all health interventions.[3] Blindness and VI due to cataract are associated with reduced quality of life[4] and visual function, which can be ameliorated following surgical management.[5] Considerable social and economic disadvantages can result from cataract, especially in poor communities, and contribute to the perpetual cycle of poverty.[6] Indeed, provision of cataract surgery may be an effective tool in poverty alleviation.[7] Management of cataract is recognised as a priority of the VISION2020: The Right for Sight global strategy that targets avoidable blindness.

Knowledge of the epidemiology of cataract is crucial for eye care programmes in sub-Saharan Africa (SSA) to effectively plan public health eye care. Since the implementation of VISION2020, several population-based blindness surveys have been conducted globally to guide the implementation, development and extension of services, which include provision for cataract surgery. Moreover, newer rapid assessment methodologies have been developed and used including the rapid assessment of avoidable blindness (RAAB), an extension of the rapid assessment of cataract surgical services.[8] We aimed to determine the recent epidemiology of blindness and VI due to cataract in SSA by investigating its prevalence and public health impact via assessment of relevant WHO targets and indicators.[3]

METHODS

Our literature search was conducted for the years 2000–October 2012 using Medline, Embase and Google Scholar. Key words used included but were not limited to: *cataract*, *lens opacity*, *visual impairment*, *low vision*, *blindness*, *presenting visual acuity*, *prevalence* and *population*. All 48 SSA African countries as well as 'Africa' and 'sub-Saharan Africa' were used in the search terms. Studies were included if they were population-based with a sample size >1000, reported presenting visual acuity (PVA) with its causes, had a high participation rate (>75%) and provided the standard WHO categories of visual acuity. We also searched reference lists of studies meeting inclusion criteria. Published studies reported in English, French and Portuguese languages were included.

Where a population-based study of blindness had taken place more than once in a single country,

data from the more recent survey (provided methodology was equivalent or superior) are presented, unless two separate geographical areas within the same country were sampled within 5 years of one another. Estimates from national surveys were used in preference to regional estimates from the same country. Both detailed population-based surveys and rapid assessment methods (rapid assessment of cataract surgical services and RAAB) were included.

Blindness was defined using WHO criteria as PVA in the better eye of <3/60 (<20/400; <1.30 LogMAR) while VI was defined as PVA in the better eye of <6/18–3/60 (<20/60–20/400; <0.48–1.30 LogMAR), representing the sum of moderate and severe VI. Thus, we did not investigate mild VI. All-cause prevalence of blindness and VI were extracted from each study as well as the proportion of blindness and VI due to cataract. Based on this information, the sample population prevalence of cataract blindness and cataract-related VI were computed using the denominator (number of persons examined), while the numerator was calculated using the proportion of blindness/VI due to cataract. We also extracted cataract surgical coverage (CSC) (at PVA<3/60 and PVA<6/18 levels for persons), visual outcomes following cataract surgery and their causes (good (PVA>6/18), borderline (6/18 to 6/60) and poor (PVA<6/60)), and per cent intraocular lens (IOL) implantation. CSC was calculated as CSC=a/(a+c) (where a=aphakic or pseudophakic, c=cataract blindness or VI). Last, we collected data on barriers to cataract surgery (unoperated subjects) and satisfaction with surgery (operated subjects).

RESULTS

Data from a total of 17 surveys from 15 different countries in SSA were included, encompassing 96 402 subjects who were examined (table 1). Most studies examined only adults aged ≥40 or ≥50 years; however, two studies included all ages,[13 15] and one ≥5 years.[14] There were two studies from Cameroon, representing one rural and one urban district.[10 11] The only other country contributing two separate published studies was Tanzania, including RAAB surveys from Kilimanjaro and Zanzibar.[20 21] Additional RAAB surveys were performed in Botswana,[9] Burundi,[22] Malawi,[17] Rwanda,[19] Eritrea[12] and Kenya.[16] Five studies were national surveys.[9 12–14 18] All studies employed cluster random sampling, with differences in the sampling used within cluster.

Blindness prevalence ranged from 0.4% in Uganda to 9.0% in Eritrea (table 2). Only two studies—Eritrea and Ethiopia—had blindness prevalence estimates exceeding 5%. Cataract accounted for between 21% of blindness in Cameroon and the highest proportion, 67%, was in Zanzibar, Tanzania. Cataract was the principal cause of blindness in 15 of 17 studies.

The prevalence of VI (sum of moderate and severe VI) ranged from 1.6% in Gambia and Uganda to 17.1% in Ghana (table 3).

Table 1 Population-based studies from sub-Saharan Africa with data on blindness and age-related cataract

Country	Level	Year published	Sampling method	Sampling within cluster	Sample size (*number examined*)	Response rate (%)	Age (years)	References
Botswana	National	2009	CRS	Compact segment sampling	2127	79.9	≥50	9
Burundi	Provincial	2012	CRS	Compact segment sampling	3684	97	≥50	22
Cameroon	Limbe	2007	CRS	Compact segment sampling	2215	92.3	≥40	10
Cameroon	Muyuku	2006	CRS	Random walk	1787	89.3	≥40	11
Eritrea	National	2011	CRS	Compact segment sampling	3163	95.9	≥50	12
Ethiopia	National	2007	CRS	Random walk	25 650	85.4	All	13
Gambia	National	2000	CRS	Compact segment sampling	13 046	92	≥5	14
Ghana	City	2012	CRS	House to house census	5603	82.3	≥40	38
Guinea	District, Bioko	2002	CRS	Household cluster sampling	3218	NS	All	15
Kenya	District, Nakuru	2007	CRS	Compact segment sampling	3503	92.6	≥50	16
Malawi	District	2011	CRS	Compact segment sampling	3430	95.7	≥50	17
Mali	Subnational	2008	CRS	Compact segment sampling	2438	NS	≥50	39
Nigeria	National	2009	CRS	Random walk	13 599	89.9	≥40	18
Rwanda	Western province	2007	CRS	Compact segment sampling	2206	98	≥50	19
South Sudan	District	2006	CRS	Random walk	2499	84.6	≥5	40
Tanzania (Kilimanjaro)	Regional	2010	CRS	Random walk	3436	95.5	≥50	20
Tanzania (Zanzibar)	Island	2007	CRS	Compact segment sampling	3160	98.8	≥50	21
Uganda	15 neighbouring villages	2002	CRS	NS	4076	98.9	≥13	41

CRS, cluster random sampling; NS, not stated.

Table 2 Prevalence and leading causes of blindness (PVA<3/60 in worse eye) in sub-Saharan Africa

Country	Bilateral blindness prevalence (95% CI)	Main cause of blindness	Proportion of blindness (%)	2nd Main cause of blindness	Proportion of blindness (%)	Prevalence of cataract blindness	References
Botswana	3.69 (2.4 to 5.0)	Cataract	47	NS	NS	1.7	9
Burundi	1.1 (0.8 to 1.4)	Cataract	55	PSED	37	0.6	22
Cameroon (Limbe)	1.1 (0.7 to 1.5)	PSED	29	Cataract	21	0.2	10
Cameroon (Muyuka)	1.6 (0.8 to 2.4)	Cataract	62	PSED and onchocerciasis	14	1.0	11
Eritrea	9.0 (8.0 to 10.0)	Cataract	55	Glaucoma	15	5.0	12
Ethiopia	7.9 (6.9 to 8.9)	Cataract	50	Trachoma	20	4.0	13
Gambia*	0.42	Cataract	45	Other corneal	16	0.2	14
Ghana†	1.2	Cataract	44	Glaucoma	22	0.5	38
Guinea	3.2 (2.6 to 3.9)	Cataract	61	Macular affection	25	2.0	15
Kenya	2.0 (1.5 to 2.4)	Cataract	42	PSED	30	0.8	16
Malawi	3.3 (2.5 to 4.1)	Cataract	48	Glaucoma	16	1.6	17
Mali	11.07 (9.55 to 12.6)	Cataract	61	Surgical complications	10	6.8	39
Nigeria	4.2 (3.8 to 4.6)	Cataract	43	Glaucoma	17	1.8	18
Rwanda	1.8 (1.2 to 2.4)	Cataract	65	PSED	20	1.2	19
South Sudan	4.1 (3.4 to 4.8)	Cataract	41	Trachoma	35	1.7	40
Tanzania (Kilimanjaro)	2.4 (1.9 to 2.9)	Cataract	51	PSED	36	1.2	20
Tanzania (Zanzibar)	3.7	Cataract	67	PSED	25	2.5	21
Uganda	0.4 (0.3 to 0.7)	Glaucoma	39	Cataract	23	0.1	41

*Estimates for ≥50 years.
†This study excludes refractive error from table of blindness/VI aetiology.
NS, not stated; PSED, posterior segment eye disease; PVA, presenting visual acuity; VI, visual impairment.

Cataract was the major cause of VI in 14 of 17 studies. The prevalence of VI due to cataract ranged from 18% to 87%.

CSC data were variable, and for blind persons ranged from 15% in Burundi to 80% in Limbe, Cameroon. This included aphakia and pseudophakia; and for patients who had received cataract surgery, between 62% and 100% had an IOL (table 4). In terms of PVA, the proportion of good outcomes ranged from 23% to 70%. Poor outcomes (VA<6/60) accounted for more than 20% in all studies and ranged from 23% to 64%.

There was a strong positive correlation between good visual outcomes and IOL use (R=0.69, p=0.027). There was an inverse correlation between IOL use and poor visual outcome

Table 3 Leading causes of visual impairment (VI) in sub-Saharan Africa

Country	Main cause of VI	Proportion of VI (%)	2nd Main cause of VI	Proportion of VI (%)	References
Botswana	Cataract	59	NS	NS	9
Burundi	Refractive error	67	Cataract	18	22
Cameroon (Limbe)	Cataract	48	Refractive error	22	10
Cameroon (Muyuka)	Cataract	40	PSED	28	11
Eritrea	Cataract	55	Refractive error	31	12
Ethiopia	Cataract	34	Refractive error	26	13
Gambia	Cataract	61 (≥50 years)	Uncorrected aphakia	12 (≥50 years)	14
Ghana*	Cataract	53*	Glaucoma	14*	38
Guinea	Cataract	87	Macular affection	29	15
Kenya	Cataract	36	Refractive error	32	16
Malawi	Cataract	46	Refractive error	41	17
Mali	Cataract	61	Refractive error	22	39
Nigeria	Refractive error	57	Cataract	26	18
Rwanda	Cataract	55	Refractive error	30	19
South Sudan	Trachoma	58	Cataract	29	40
Tanzania (Kilimanjaro)	Cataract	55	Refractive error	33	20
Tanzania (Zanzibar)	Cataract	47	Refractive error	39	21
Uganda	Cataract	57	Refractive error	19	41

VI 6/18 to 3/60.
*This study excludes refractive error from table of blindness/VI aetiology.
NS, not stated; PSED, posterior segment eye disease.

Table 4 CSC, visual outcomes following cataract surgery and per cent IOL use in sub-Saharan Africa

	CSC (VA<6/18) persons			CSC (blind persons (PVA<3/60))			Visual outcome (PVA)		
Country	Total persons	Males	Females	Total persons	Male	Female	Good (PVA>6/18)	Poor (PVA<6/60)	IOL (% of all operated eyes)
Botswana	53	62	48	62	73	55	NS	NS	NS
Burundi	12	9	13	22	17	24	70	30	100
Cameroon (Limbe)	NS	NS	NS	80	NS	NS	23	58	69
Cameroon (Muyuka)	NS	NS	NS	55	NS	NS	25	64	68
Eritrea	48	50	46	68	71	65	41	39	75
Kenya	51	51	51	78	78	78	50	31	58
Malawi	16	25	10	45	62	30	41	32	68
Mali	34	39	30	59	70	51	28	58	33
Nigeria	NS	NS	NS	NS	NS	NS	30	41	40
Rwanda	21	24	19	47	64	36	24	41	62
Tanzania (Kilimanjaro)	42	48	37	70	73	67	59	23	87
Tanzania (Zanzibar)	20	25	17	60	77	49	32	38	68

No data were available from Ethiopia, Ghana, Guinea, South Sudan and Uganda.
CSC, cataract surgical coverage; IOL, intraocular lens; NS, not stated; PVA, presenting visual acuity.

(R=−0.31, p=0.384). There was an inverse relationship between the proportion of blindness due to cataract and CSC (persons, blindness; R=−0.50, p=0.137). There was an inverse relationship between CSC (blind) and good visual outcome (R=−0.34, p=0.37).

The causes of a poor visual outcome, barriers to cataract surgery and satisfaction rates with surgery were identified (table 5). Insertion of an IOL is consistently associated with having a good visual outcome. Lack of awareness and inability to pay were frequently cited as major barriers to cataract surgery. The majority of individuals surveyed reported being satisfied with their surgery.

DISCUSSION

We have provided an up-to-date review on blindness and VI due to cataract in SSA obtained from 17 studies of nearly 100 000 individuals. Wide differences in estimates of blindness and VI prevalence due to cataract were evident in this study, but cataract remains the principal cause of blindness in SSA. Although cataract prevalence is high in some Asian and South American populations it is on average lower than Africa and much lower in areas of higher HDI.[23]

Unsurprisingly, the population with the lowest blindness prevalence in this study, Uganda, has had a strong recent history of successful eye care programme delivery. The differences between countries are striking: a 74-fold difference in cataract blindness prevalence between Uganda and Mali who have similar GDP (per capita) of US$487 and US$669, respectively (World Bank 2011). Successful blindness prevention programme delivery and available cataract surgical services and human resources especially in rural areas, shorter distances and easier transport for patients, affordable fee structures or free services, and cultural barriers to service access may account for these huge differences. Further studies are required to quantify the resources required to make such differences and to examine how this has been achieved.

It has been suggested that a cataract surgical rate (CSR) of ≥2000 operations/million population/year should be achieved annually to eliminate unnecessary blindness due to cataract in Africa.[24] This benchmark is in stark contrast to the current situation in many parts of Africa, with over 80% of WHO member states in Africa having a CSR<1000.[3] A substantial increase in CSR is needed to reduce blindness and VI due to cataract in SSA. Worse HDI ranks are associated with a higher prevalence of cataract blindness, and in SSA a much higher proportion of individuals undergoing surgery for cataract have preoperative blindness or SVI compared with higher-income populations.[25] The challenge remains reaching blind and visually impaired people by providing accessible, affordable and sustainable cataract surgical services.

Importantly, any increase in cataract surgical output is usually accompanied by an increase in outcome. The proportion of good outcomes ranged from 23% to 70%, all of which fail to reach WHO target that ≥85% of eyes should achieve PVA<6/18 postoperatively. These proportion of good visual outcomes in most studies were markedly lower than from recent hospital-based studies on this continent.[26 27] Prospective monitoring of outcomes can improve quality,[28] with a dynamic and learning process for the surgeon of focusing on reducing surgical complications, greater emphasis on appropriate selection, need for spectacle correction and sequelae of surgery. In many settings, non-physician cataract surgeons provide the majority of cataract surgery. There remains controversy as to whether this cadre of surgeons is ideal to meeting the cataract surgical needs in SSA. Greater regulation and long-term training of physician-surgeons may provide a better long-term solution.

Population-based data on visual outcomes are highly valuable as clinic/hospital-based outcome estimates are not often representative of the visual status in the community. However, as modern techniques using extra-capsular cataract extraction with IOL implantation are now ubiquitous in almost all areas of SSA, population-based outcomes are likely to be worse as they may capture outcomes for surgeries performed many years prior (eg, intracapsular cataract extraction). Uncorrected aphakia remains an important contributor to blindness and VI in many areas of SSA.[29] More recently, performed cataract surgery is associated with more frequent use of IOL,[16 30] which in turn is positively correlated with a good visual outcome. In some areas, cataract removal by couching leading to aphakia is associated with extremely poor visual outcomes, even with aphakic correction.[31]

Poor visual outcomes ranged from 23% to 64%, with the causes of poor outcomes being variable, and representing differences in expertise, resources and monitoring/surveillance. Understanding the causes of such poor outcomes is vital. Visual outcomes can be ameliorated with improved case selection and avoidance of surgery in patients who will not benefit; improving

Table 5 Causes of poor outcome and barriers to cataract surgery in studies with available data in sub-Saharan Africa

Country	Causes of poor outcome: Selection/ comorbidity	Causes of poor outcome: Surgical complications	Causes of poor outcome: Uncorrected refractive error, aphakia, late sequelae	Associations with poor outcome	Barriers to surgery	Satisfaction with surgery (postoperative subjects)
Cameroon (Limbe)	NS			Aphakia (compared with IOL use) Older age	Inability to pay (40%), lack of awareness (17%), a feeling they could cope with the cataract (10%) and that they were waiting for cataract to mature (8%)	NS
Cameroon (Muyuka)	NS			Aphakia (compared with IOL use) Older age	Lack of awareness of cataract (33.3%), inability to pay (30.1%) and a feeling they could cope with the cataract (9.6%)	NS
Eritrea	27%	24%	48%	Having surgery performed at a voluntary or charitable hospital compared with a government hospital	30% reported 'Cannot afford', followed by 'Waiting for maturity' (18%), 'No company' (17%), 'Contra-indication' (12%) and 'Old age, no need' (10%)	NS
Kenya	36%	30%	34%	Not specified for poor outcome However, good outcome was more likely if the surgery was with an IOL, performed in last 5 years or undertaken in a volunteer/charity hospital or private hospital rather than a government hospital or eye camp	'Not aware of surgery' (34.1%), 'cannot afford the operation' (24.4%) and 'no one to take me' (12.2%)	64% were very satisfied, 19% were somewhat satisfied, 5% were indifferent, and 12% were somewhat or very dissatisfied
Malawi	40%	47%	13%	NS	Old age ('no need felt') was reported to be the commonest barrier (23.5%) followed by 'no one to accompany' (22.1%), 'no services nearby' (13.2) and 'unaware that treatment was available' (11.8%)	84.8% of all persons who had surgery were either very satisfied or partially satisfied. Only 3% of persons were very unsatisfied with the results of surgery
Nigeria NB: Barriers refers to Abubakar *et al*[42]	NS This refers to: Imam *et al*[30]	19%	50%	In multivariate analysis of data on first-operated eyes, the only variable associated with poor outcome (<6/60 at presentation) was non-IOL surgery	Cost of surgery (over a third), other personal factors (a quarter), and another quarter cited barriers such as being too old, not knowing where to go and fear of surgery. Provider-related factors, such as being told to attend later, were reported by 9.8% There were significant rural–urban differences in cost as a barrier	NS
Rwanda	25%	50%	25%	NS	Lack of awareness of the availability of treatment (52%), followed by a perceived lack of services (16%), inability to afford the surgery (16%) and lack of a companion (8%)	41% were very satisfied, 28% were partially satisfied, indifferent (7%), partially dissatisfied (17%) or very dissatisfied (7%)
Tanzania (Kilimanjaro)	31%	38%	25%	Eyes with an IOL had significantly better vision than eyes without	NS	NS
Tanzania (Zanzibar)	The major cause of poor outcome for operations >3 years ago was selection and presently it is due to sequelae Surgery was a major cause for poor outcome for both time periods			NS	Unaware of treatment (30%), waiting for cataract to mature (20%) and cost (10%)	56% very satisfied, 25.9% partially satisfied, 7.9% very dissatisfied

IOL, intraocular lens; NS, not stated.

the quality of surgery and avoiding surgical complications; improving the operative (IOL) and/or postoperative correction of refractive error and; and reducing late postoperative complications.[32] Further cataract surgery outcomes data are needed from studies in SSA, and globally, to assess not only the importance and complexity of good outcomes and to revisit the parameters set by WHO, but most importantly to understand and disseminate knowledge about how to improve outcomes.

It is intuitive that in order to reduce the blindness and VI due to cataract the CSR needs to exceed the cataract incidence rate. Lewallen *et al* have modelled the incidence of vision-reducing cataract in Africa using data from RAAB surveys.[33] Such derived estimates may assist further with the planning of services in this resource-poor region where incidence estimates are scarce and have indicated disparities in cataract incidence in this continent. WHO recommends the establishment of ≥1 cataract unit per district of a million population in order to deal with cataract blindness and VI.[3] CSRs also reflect variations in genetic, environmental, or cultural factors and will vary with population structure, which is not uniform across Africa.[33]

Two indicators can measure the impact of initiatives to target cataract. First, performing serial cross-sectional population-based surveys to demonstrate evidence of a reduction in prevalence of cataract (and blindness and VI due to cataract) over time.[14 34] Another indicator is to measure the CSC which represents a ratio of the met and unmet need for cataract surgery and is a measurement of the capability of a healthcare system to provide cataract surgical services to the population.[35] In these studies, the CSC for persons for blinding cataract ranged from 22% to 70%, and was usually higher in men reflecting probably gender inequity in access to cataract surgical services.[36] CSR is positively correlated with CSC,[25] but CSC does not take into account the quality of surgery provided.

There are several limitations to this review. Inter-study differences exist with relation to the size, age/gender composition, response rates and degree of urbanisation as well as degree of government and non-government organisation involvement in the surveyed areas. Such differences may account for some of the heterogeneity between individual results. RAAB surveys have several disadvantages including their lack of detailed cataract phenotype information. Nonetheless, the validity of the RAAB compared with a more detailed survey is high.[37]

In conclusion, cataract is by far the most common cause of blindness and VI in SSA. Efforts to reduce the burden of blindness and VI due to cataract should incorporate high-volume, high-quality, affordable cataract surgery that greatly improves the CSR and CSC in such populations. This can be achieved by the implementation of well-run, cost-effective and sustainable cataract units at the district level. Wide variation in the prevalence of cataract blindness has been shown in this review, and although this may be due to disparities in eye care programme delivery, it may also reflect inter-population differences in cataract incidence. The fundamental problems highlighted by this review are that currently too few cataract surgeries are being performed and there are too many poor outcomes. An open and urgent appraisal of positive successes throughout SSA should be performed and shared.

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Blindness and visual impairment due to age-related cataract in sub-Saharan Africa: a systematic review of recent population-based studies

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Chapter 3. Posterior segment eye disease in sub-Saharan Africa: review of recent population-based studies

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Thesis Title	The Nakuru Eye Disease Cohort Study

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Posterior segment eye disease in sub-Saharan Africa: review of recent population-based studies

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Abstract

OBJECTIVE To assess the burden of posterior segment eye diseases (PSEDs) in sub-Saharan Africa (SSA).
METHODS We reviewed published population-based data from SSA and other relevant populations on the leading PSED, specifically glaucoma, diabetic retinopathy and age-related macular degeneration, as causes of blindness and visual impairment in adults. Data were extracted from population-based studies conducted in SSA and elsewhere where relevant.
RESULTS PSEDs, when grouped or as individual diseases, are a major contributor to blindness and visual impairment in SSA. PSED, grouped together, was usually the second leading cause of blindness after cataract, ranging as a proportion of blindness from 13 to 37%.
CONCLUSIONS PSEDs are likely to grow in importance as causes of visual impairment and blindness in SSA in the coming years as populations grow, age and become more urban in lifestyle. African-based cohort studies are required to help estimate present and future needs and plan services to prevent avoidable blindness.

keywords glaucoma, diabetic retinopathy, age-related macular degeneration, posterior segment eye disease, prevalence, incidence, blindness, visual impairment, Africa

Introduction

Non-communicable diseases in low- and middle-income countries

In recent decades, there has been a marked rise in life expectancy that has contributed to a major epidemiological shift in populations worldwide (Lopez *et al.* 2006). These changes will increasingly lead to major public health issues in low- and middle-income countries (LMIC; Mathers & Loncar 2006). Current projections suggest that non-communicable diseases (NCDs) will contribute to two-thirds of global mortality by the year 2030 (Mathers & Loncar 2006). NCDs in LMIC have shown substantial variation in prevalence, incidence, natural history and risk factors compared with NCDs in populations in high-income countries (Boutayeb 2006).

Visual impairment and blindness

285 million people are visually impaired (VI) worldwide, (severe visual impairment (SVI) defined as presenting visual acuity (PVA) <6/60 but ≥3/60, moderate VI defined as PVA <6/18 but ≥6/60) of whom 39 million are blind (presenting visual acuity <3/60 in the better eye; Pascolini & Mariotti 2012). Approximately 90% of those worldwide with VI live in low-income countries. NCDs are the leading causes of VI, in part due to the successful control of infectious diseases. VI is ranked sixth in the top ten causes of burden of disease in terms of disability-adjusted life-years (DALYs) in low-income, middle-income and high-income countries (Chiang *et al.* 2006). The sum of DALYs from VI is 66 290 000 (4.3% of total), just below HIV/AIDS at 71 460 000 (4.7%).

The number of people visually impaired in the World Health Organization (WHO) African region is estimated to be 26 million, of whom almost 6 million are blind. This is based on estimates from population-based studies in Botswana, Cameroon, Eritrea, Ethiopia, Gambia, Ghana, Kenya, Mali, Nigeria, Rwanda, Uganda and Tanzania (Pascolini & Mariotti 2012). Despite Africa having one of the highest prevalences of blindness, it is the most underserved continent in terms of human resources

available to treat and manage eye disease (Resnikoff *et al.* 2012), with the greatest gap between existing need and provision (Bastawrous & Hennig 2012).

In 2010, the WHO reported the leading causes of visual impairment (VI) and blindness (Pascolini & Mariotti 2012). Of these, three of the nine listed leading causes are NCDs which are posterior segment in location, (i.e. affecting the back of the eye). Posterior segment eye disease (PSED) epidemiologically is commonly defined as diseases of the retina, choroid and optic nerve and primarily includes: glaucoma, age-related macular degeneration (AMD) and diabetic retinopathy (DR). These three conditions are the focus of this paper but do not constitute all PSEDs. See Figure 1.

PSED and VISION2020

VISION2020 is the global initiative for the elimination of avoidable blindness, launched in 1999, jointly by WHO and the International Agency for the Prevention of Blindness (IAPB) and provides technical support and advocacy to prevention of blindness activities worldwide. It aims over two decades to prevent 100 million people from becoming blind.

VISION2020 has largely focused on the elimination of anterior segment diseases, primarily cataract, as it alone causes almost half of blindness and is amenable to cure through surgery. VISION2020 has not focused on PSED to date mostly due to a lack of data on the magnitude of these conditions and lack of cost-effective treatment options. This review aims to establish the magnitude of visual impairment and blindness in SSA that can be attributed to PSED.

Materials and methods

Our literature search was conducted for the years 1966 to September 2012 using PubMed. Keywords used included the following: posterior segment eye disease, glaucoma, age-related macular degeneration, diabetic retinopathy, correctable visual impairment, preventable, avoidable, Africa (MeSH), aphakia, blindness, visual impairment, prevalence and population.

Studies were selected for inclusion if they were population based, performed in sub-Saharan Africa with a sample size >1000, reported visual acuity impairment with its causes, had a high participation rate (>80% of the targeted sample) and presented results using the standard WHO categories of VA. WHO definitions of visual impairment are used (WHO/ICD-10 2007). We also searched reference lists of studies meeting inclusion criteria. Only published data were included.

All-cause prevalence (and 95% confidence interval [CI]) of blindness, SVI and moderate VI was extracted from each study, as well as the proportion of blindness, SVI and moderate VI due to PSED (grouped or as single diseases when available); then, the prevalence of blindness, SVI and moderate VI due to PSED was calculated from these estimates.

Results

Search results

In total, the initial search criteria identified 112 potential manuscripts for inclusion. Review of the abstracts reduced this to 39 potential studies, of which 17 surveys, from 13 SSA countries, encompassing 88 067 individuals were included for analysis having fully met the pre-specified search criteria. Data from the following countries are presented: Burundi (Kandeke *et al.* 2012), Cameroon (Oye *et al.* 2006; Oye & Kuper 2007), Eritrea (Muller *et al.* 2011), Ethiopia (Berhane *et al.* 2007), Ghana (Budenz *et al.* 2012), Guinea (Moser *et al.* 2002), Kenya (Mathenge *et al.* 2007a, 2012), Malawi (Kalua *et al.* 2011), Nigeria (Adegbehingbe *et al.* 2006; Abdull *et al.* 2009), Rwanda (Mathenge *et al.* 2007b), South Sudan (Ngondi *et al.* 2006), Tanzania (Kikira

Figure 1 Cross-sectional diagram of the eye demonstrating the anterior and posterior segments and their potential diseases.

2007; Habiyakire *et al.* 2010) and Uganda (Mbulaiteye *et al.* 2002).

Posterior segment eye disease

Although PSEDs are frequently collated in SSA-based epidemiological studies and presented as a single entity or group of conditions, they are clinically and pathophysiological distinct. The most common methodological approach deployed in SSA population-based studies, the rapid assessment of avoidable blindness (RAAB; Dineen *et al.* 2006), is not sufficiently sensitive to differentiate posterior segment causes of low vision and hence presented results are often collated.

Posterior segment eye disease in Africa

Cross-sectional population-based studies from the last two decades performed in Africa have shown PSED to be consistently the second (and occasionally the most common) leading cause of blindness. This includes studies from Kenya (Mathenge *et al.* 2007a, 2012), Nigeria (Rabiu & Muhammed 2008; Abdull *et al.* 2009), Tanzania (Kikira 2007; Habiyakire *et al.* 2010), Rwanda (Mathenge *et al.* 2007b), Cameroon (Oye *et al.* 2006; Oye & Kuper 2007), Ghana (Guzek *et al.* 2005), Guinea (Moser *et al.* 2002), Burundi (Kandeke *et al.* 2012) and Ghana (Budenz *et al.* 2012; See Table 1). No longitudinal data on PSED from population-based studies in Africa have been published. A single cohort in Uganda has 3-year cumulative incidence data on visual impairment, (age-standardised incidence rate of 13.2, per 1000 PY) with AMD and glaucoma amongst the leading causes of visual loss in new cases (Mbulaiteye *et al.* 2003). However, no baseline clinical phenotyping data were collected in eyes initially without visual impairment, so early asymptomatic disease was not excluded.

The majority of available prevalence data in Africa come from the rapid assessment of avoidable blindness (RAAB) methodology (Dineen *et al.* 2006). Although RAAB is a validated survey method (Mathenge *et al.* 2012), it has a limitation in common with more comprehensive surveys such as the Nigeria study (Dineen *et al.* 2008) in that detailed eye examinations are only performed in those found to have impairment of their visual acuity. As glaucoma patients usually lose central vision at the end stage of the disease, they are frequently missed unless visual field assessment is performed. Furthermore, ophthalmic assessment in RAAB relies on direct ophthalmoscopy, constraining diagnostic accuracy, so that the diseases are pragmatically grouped together as one unit.

The majority of these surveys have used the WHO coding instructions, which use the 'principal disorder responsible for visual loss in the individual after considering disorders in either eye which are most amenable to treatment or prevention' (World Health Organization 1988). In other words, if a patient has PSED coexistent with cataract, it will be deemed that cataract is the primary cause of blindness/VI. Therefore, most VI prevalence data available in which cataract or refractive error is the primary cause will underestimate the prevalence of PSED at all levels of visual acuity.

Glaucoma in Africa

Prevalence. Current estimates suggest that there are 6.5 million people with glaucoma at all levels of vision in sub-Saharan Africa (SSA) with a projected increase to 8.4 million in 2020 (Quigley & Broman 2006). Glaucoma is estimated to be the second leading cause of blindness in Africa (Cook 2009). These estimates undertaken by Quigley and Broman (2006) are based on seven population-based studies, of which two examined individuals of African descent living outside of the African continent: in Baltimore, USA (Leske *et al.* 1994) and Barbados (Tielsch *et al.* 1991a) which has multiple limitations for inferring data. Of the five based in Africa, three were undertaken in South Africa (Salmon & Martell 1994; Rotchford & Johnson 2002; Rotchford *et al.* 2003), one in Ghana (Ntim-Amponsah *et al.* 2004) and one in Tanzania (Buhrmann *et al.* 2000). The studies used varying sampling methods and criteria for diagnosis of glaucoma.

No specific and sensitive test for glaucoma exists. Current reference standard diagnosis requires expensive visual field-testing equipment with expert interpretation of the optic disc and visual field findings. Standardised definitions and classifications of glaucoma in recent years have allowed for better prevalence estimates and comparisons between populations (Foster *et al.* 2002).

Glaucoma may be congenital or acquired and further subclassified into open-angle and closed-angle based on the mechanism by which aqueous outflow from the eye is compromised. The 'angle' refers to the junction between cornea and iris, which forms an angle of varying degree in each eye. Generally speaking, in glaucoma, when this angle is large and the structures within it are visible on clinical examination (gonioscopy), it is termed 'open-angle glaucoma' and when these structures are limited or not visible due to a narrow angle, it is termed 'closed- or narrow-angle glaucoma' (Kanski 2007). Primary open-angle glaucoma (POAG) disproportionately affects individuals of African descent (Quigley & Broman 2006)and is difficult to diagnose in early disease, and when

Table 1 Reviewed studies

Country	Level	Year published	Sample size *(number examined)*	Response rate (%)	Age (years)	Primary cause of blindness	Secondary cause of blindness	Equipment used for diagnosis	References
Burundi	Provincial	2012	3684	97	≥50	Cataract (55%)	PSED (37%)	Not stated	Kandeke *et al.* (2012)
Cameroon	Limbe	2007	2215	92.3	≥40	Cataract (62%)	PSED (25%)	Direct ophthalmoscope	(Oye and Kuper (2007)
Cameroon	Muyuka	2006	1787	89.3	≥40	PSED (29%)	Cataract (21%)	Direct ophthalmoscope	Oye *et al.* (2006)
Eritrea	National	2011	3163	95.9	≥50	Cataract (55%)	Glaucoma (15%)	Portable slit lamp	Muller *et al.* (2011)
Ethiopia	National	2007	25650	85.4	All	Cataract (50%)	Trachoma (8%)	Direct ophthalmoscope	Berhane *et al.* (2007)
Ghana	City	2012	5603	82.3	≥40	Cataract (44%)	Glaucoma (22%)	Slit lamp/fundus camera	Budenz *et al.* (2012)
Guinea	District, Bioko	2002	3218	NS	All	Cataract (61%)	Macular Affection (21%)	Slit lamp	Moser *et al.* (2002)
Kenya	District, Nakuru (RAAB)	2007	3503	92.6	≥50	Cataract (42%)	PSED (30%)	Direct ophthalmoscope	Mathenge *et al.* (2007)
Kenya	District, Nakuru	2012	4414	88.1	≥50	Cataract (45%)	PSED (32%)	Slit lamp/fundus camera	Mathenge *et al.* (2012)
Malawi	District	2011	3430	95.7	≥50	Cataract (48%)	Glaucoma (16%)	Direct ophthalmoscope	Kalua *et al.* (2011)
Nigeria	National	2009	13599	89.9	≥40	Cataract (43%)	Glaucoma (17%)	Slit lamp/fundus camera	Abdull *et al.* (2009)
Nigeria	Local Government Area	2008	2424	93.6%	≥50	Cataract (46%)	Surgical complications (20%)	Direct ophthalmoscope	Rabiu (2008)
Rwanda	Western province	2007	2206	98	≥50	Cataract (65%)	PSED (20%)	Direct ophthalmoscope	Mathenge *et al.* (2007)
South Sudan	District	2006	2499	84.6	≥5	Cataract (41%)	Trachoma (35%)	Torch	Ngondi *et al.* (2006)
Tanzania (Kilimanjaro)	Regional	2010	3436	95.5	≥50	Cataract (51%)	PSED (36%)	Direct ophthalmoscope	Habiyakire *et al.* (2010)
Tanzania (Zanzibar)	Island	2007	3160	98.8	≥50	Cataract (67%)	PSED (25%)	Direct ophthalmoscope	Kikira (2007)
Uganda	15 neighbouring villages	2002	4076	98.9	≥13	Glaucoma (39%)	Cataract (23%)	Direct ophthalmoscope	Mbulaiteye *et al.* (2002)

NS, Not stated. RAAB, rapid assessment of avoidable blindness, PSED, posterior segment eye disease.
All studies were cross-sectional, population-based studies, which used cluster random sampling.

diagnosis is confirmed, there is still debate on the best management in the context of limited resources and prospects for long-term follow-up (Quigley *et al.* 2000). Narrow-angle glaucoma prevalence is not well reported in African populations, this is in large part due to gonioscopy not being performed in the frequently used RAAB methodology and also in other more comprehensive surveys (Mathenge *et al.* 2012).

People of African descent (not living in Africa) have a higher prevalence of glaucoma, are more likely to develop glaucoma at an early age with more aggressive disease and have a higher risk of glaucoma related blindness than Caucasians or Asians (Mason *et al.* 1989; Tielsch *et al.* 1991b). It is therefore vital that the epidemiology of glaucoma is investigated in more detail in various populations in Africa.

Comprehensive reviews on glaucoma in Africa were published in 2009 (Cook 2009) and 2013 (Kyari *et al.* 2013), no new data from African population-based studies have since been published since 2009. The authors are aware of awaited data to be published from study groups in Nigeria (Dineen *et al.* 2008), Ghana and Kenya (Mathenge *et al.* 2012).

Current data on glaucoma underestimate the true prevalence, as many cases of glaucoma have preservation of central vision and do not include visual field assessment (Cook 2009). Furthermore, preferential coding of cataract due to its reversible nature often means that glaucoma is not assigned as the primary cause of blindness in a patient with visual loss from coexistent glaucoma and lens opacity, as per WHO criteria (World Health Organization 1988).

Incidence. It is assumed that incidence of glaucoma in Africa will most closely reflect that of the Barbados Eye Study, whose enrolled participants were of West African descent (Leske *et al.* 2001, 2007). All other studies with data on glaucoma incidence have been conducted in largely Caucasian populations: the Ponza Eye Study (Cedrone *et al.* 2012), the Dalby Eye Study (Bengtsson 1991), the Blue Mountain Eye Study (Chandrasekaran *et al.* 2006), the Melbourne Visual Impairment Study (Dimitrov *et al.* 2003) and the Rotterdam Eye Study (de Voogd *et al.* 2005). Annual incidence of new glaucoma in these studies varied from 0.1 to 0.6%, the highest being in the Barbados Eye Study which was largely made up of people of African descent. To date, no data on incident glaucoma or glaucoma progression from population-based studies in Africa are available.

Diabetic retinopathy in Africa

Prevalence. Diabetes is a major threat to global public health. The estimated prevalence of diabetes worldwide was 285 million in 2010, representing 6.4% of the world's adult population, with a prediction that by 2030 there will be 438 million people with diabetes (DF 2009). The most substantial increases (7 to 15 million, 111%) are expected to be in Africa and the Middle East as a result of various factors including population growth, ageing, urbanisation, dietary changes and the increase in obesity and sedentary lifestyles in these regions (King & Herman 1998).

Although no data exist from population-based studies (PBS) in Africa directly comparing ethnic variation as a risk for DR, a hospital-based study in South Africa estimated the prevalence of DR amongst patients with adult-onset diabetes attending a large community hospital to be similar in patients of African (37%), European (41%) or Indian (37%) heritage. However, 'severe DR' (study specific classification) was significantly more frequent in Africans (52%) and Indians (41%) than Europeans (26%; Kalk *et al.* 1997). The predicted rise in proportion of adults suffering from diabetes will inevitably lead to an increase in the prevalence of DR (Williams *et al.* 2004).

The detection of DR in Africa remains a challenge in part due to a lack of necessary equipment and skilled manpower (Rotimi *et al.* 2003). The authors of this review [also cited in reference: (Burgess *et al.* 2013)] identified two high-quality, population-based, cross-sectional studies reporting DR prevalence in Africa (but not SSA). The Diabetes in Egypt project (1993; Herman *et al.* 1998) reported the proportion of DR and PDR in individuals with diabetes to be 31.6% and 0.9%, respectively. The Mauritius diabetes complication study (Dowse *et al.* 1998) reported 30.2% DR and 1.3% PDR; the prevalence of PDR in subjects with known diabetes was 2.3%. These figures are comparable with prevalence estimates reported in recent American and European studies.

Egypt and Mauritius are ethnically and demographically very different to most countries of sub-Saharan Africa; the findings of these studies should be generalised to other settings with caution.

There are also estimates of the prevalence of DR amongst diabetics from high-quality clinic-based studies in Africa. Very high prevalences of DR, PDR and maculopathy have been reported. A study from Malawi reported 32.0% DR, 5.7% PDR, 15% sight-threatening maculopathy (Glover *et al.* 2012). Two separate studies from South Africa have found comparable results: Mash *et al.* found 62.4% DR, 6.1% PDR and 15.2% with any maculopathy (Mash *et al.* 2007); Rotchford *et al.* found DR 40.3%, PDR 5.6%, 10.3% CSME (Rotchford 2002).

Evidence from unpublished data supports urbanisation as a risk factor for DR. Slit-lamp assessment of the retina assessing DR in a South-African PBS (Rotchford &

Johnson 2002; Rotchford *et al.* 2003) demonstrated a 0.7% prevalence of DR (NPDR 0.6%, PDR 0.1%) in rural communities and a 2.1% prevalence of DR (NPDR 1.8%, PDR 0.3%) in urban communities (A. Rotchford, unpublished data).

Estimates of the proportion of African patients with diabetes who are visually impaired are high even compared with older European and American studies. The population-based Nigerian national blindness and visual impairment survey was conducted between 2005 and 2007 (Abdull *et al.* 2009). DR was identified as the primary cause of visual impairment in 0.29% of 3129 subjects with uncorrected VA worse than 6/12 and in 0.5% of those with acuity less than 3/60. This study is likely to underestimate the visual impact of DR as examiners were instructed to preferentially record treatable, rather than preventable, causes of visual impairment.

Incidence. No population-based cohort study was identified providing incidence data on DR in SSA. However, two cohort studies of DR in Africa were identified by this review, one of which was in SSA. A survey of diabetes complications in Mauritius was followed up 6 years later (Dowse *et al.* 1998). Of subjects with diabetes in the initial survey 40.5% were re-examined for DR (Tapp *et al.* 2006). Six-year incidence of DR was 23.8%. Duration of diabetes and fasting blood glucose were independently associated with incidence of retinopathy. Six-year progression to PDR was reported from no DR (0.4%), mild NPDR (5.2%) and moderate NPDR (29.4%).

In South Africa, a cohort of patients with insulin-dependent diabetes mellitus (IDDM) diagnosed before age 30 years was followed up over time (Gill *et al.* 1984). In those subjects seen after 10 years of follow-up, prevalence of DR had increased from 6% to 52% and PDR from 0 to 3% (Gill *et al.* 1995). In subjects seen at 20 years, prevalence of DR had increased from 12% to 59%. No incidence data were collected (Gill *et al.* 2005).

No other prospective cohort studies were identified. However, a study reflecting cumulative incidence of DR from South Africa (Distiller *et al.* 2010) reported on 1520 type 1 and 8026 t ype 2 patients who had maintained membership for ≥5 years in a community-based, privately funded diabetes management programme. In type 1 participants, the prevalence of any retinopathy at baseline and at 5 years was 22.3% and 28.0%, respectively, and in type 2 participants 20.5% and 26.6%, respectively.

Age-related macular degeneration in Africa

Prevalence. The majority of data globally on AMD are from Caucasians and Asian populations (Vingerling *et al.* 1996; Cruickshanks *et al.* 2001; Buch 2005; Buch *et al.* 2005; Munoz *et al.* 2005; Arnarsson *et al.* 2006; Chen *et al.* 2008; Yasuda *et al.* 2009; Choudhury *et al.* 2011) with a paucity of data from peoples of African descent. Data on Africans are largely from studies undertaken in African populations living outside of the African continent (Leske *et al.* 2004, 2007). Comparative data between Caucasians and Africans living in the same geographical area have suggested differing predispositions towards AMD (Sommer *et al.* 1991). A single population-based study based in SSA (Kenya) determining the prevalence of AMD was identified (Mathenge *et al.* 2013). Early and late AMD prevalence in adults aged 50 years and above was 11.2% and 1.2%, respectively, amongst participants graded on digital retinal images (n = 3,304). After controlling for age, women had a higher prevalence of early AMD than men (odds ratio 1.5; 95% CI, 1.2–1.9), and the overall prevalence rose significantly with each decade of age (Mathenge *et al.* 2013).

Incidence. The incidence of AMD has been reported in population-based studies in the Americas, Australasia, Europe, and Asia; however, no data exist from the African continent to date. With the exceptions of the Latino Eye Study (Varma *et al.* 2010) and the Barbados Eye Study (Leske *et al.* 2004, 2006), all data are in Caucasian populations, and inferred data from the Barbados study suggest incident early AMD is similar to elsewhere in the world, but late AMD is less common, possibly suggesting a protective mechanism.

Discussion

We found through our review of the literature that PSEDs are an important cause of vision loss in SSA countries. Selection bias may have led to information from French- and Portuguese-speaking countries being omitted; data from Egypt and Mauritius are unlikely to be representative for the SSA, and data not in the peer-reviewed literature were also omitted and may have been a source of bias.

The detection of and treatment for PSED poses many challenges to countries that currently lack the necessary infrastructure and resources. VISION 2020 has placed priority on conditions deemed more straightforward to treat, and this strategy has proven largely successful.

PSEDs differ from the leading anterior segment eye diseases (cataract and refractive error) in prevention/treatment, as no cures currently exist (with the exception of angle closure glaucoma). Surgical intervention can restore vision in those visually impaired from cataract, and

provision of glasses can restore or improve vision in people with refractive error. However, established visual loss from PSED is difficult to reverse, and for most conditions, there is no 'curative' treatment.

Medical and/or surgical intervention for glaucoma can slow disease progression and thereby reduce the risk of further sight loss (Heijl *et al.* 2002). Systemic control of diabetes mellitus, retinal laser treatment, intravitreal injections and vitreoretinal surgery in sight-threatening DR can stabilise and, to some degree, improve DR status and thereby also prevent sight loss (1993). Currently no cure for AMD exists, although intravitreal therapy is available for end-stage wet AMD (approximately 10% of all AMD cases). The infrastructure required to detect AMD and deliver treatment as well as the cost of treatment itself is currently prohibitively expensive for use in most LMIC settings but is widely used in high-income countries (Bowler *et al.* 2012). Vitamin supplementation has shown some evidence of risk reduction in progression of subtypes of AMD (Evans 2006), but not prevention of AMD (Evans & Lawrenson 2012) and again may be prohibitively expensive.

This review suggests that PSEDs account for a large proportion of people with vision loss living in SSA. In recent years, improved methodologies and understanding may account for some increase in estimates of prevalence. In particular, the affordable RAAB methodology (Dineen *et al.* 2006) has led to increased numbers of researchers undertaking population-based surveys in SSA.

The majority of existing data on NCDs, including PSED, from LMIC are from cross-sectional studies providing valuable data on prevalence and risk factors. Longitudinal studies provide the opportunity to investigate the natural history of diseases, which is necessary in developing health policies at local and national levels. Few longitudinal cohort studies from LMIC have been conducted due to barriers including expense, complex logistical planning and political challenges.

A change in the focus of programme managers and policymakers over the coming decades is required if the prevalence and incidence of PSED in SSA increases as predicted. This increase is likely with extended life expectancies and success of the VISION 2020 in the treatment for anterior segment eye diseases and infectious diseases of the eye. Urbanisation and westernised lifestyles may also play a role in diseases such as diabetes and consequently DR.

Many studies worldwide have collected cross -sectional survey data on PSED prevalence; however, few studies have data on incident PSED with no SSA-based eye disease cohort studies to date. The best estimates of incidence for Africa are therefore extrapolated from studies conducted elsewhere in the world. Furthermore, investigating PSED in Africa offers a new perspective on account of the different exposures and genetic make-up of these populations compared with those studied thus far, which may reveal new insights into the cause and natural history of these diseases.

Inferring data from high-income countries undermines efforts to establish studies in LMIC, which will guide the effective use of minimal existing resources to deal with the growing burden of NCDs.

Large, community-based cross-sectional and cohort studies are needed to estimate prevalence of disease, risk factors for disease, as well as incidence and progression across Africa. Evidence for effectiveness and economics of screening of and treatment for PSED in low resource settings is vital for health service planners.

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Chapter 3.1. Cataract and Posterior segment eye disease in sub-Saharan Africa – update

Since the publication of the review papers (chapters 2 and 3), further population based cross sectional prevalence studies have been undertaken in SSA.

In order to update the published reviews, the same search methodology (adapted for years of publication) was used as per the reviews in Chapters 2 and 3 which was:

Our literature search was conducted for the years 2012 – April 2017 using Medline, Embase and Google Scholar. Key words used included but were not limited to: *cataract, lens opacity, glaucoma, macula degeneration, diabetic retinopathy, visual impairment, low vision, blindness, presenting visual acuity, prevalence,* and *population*. All 48 SSA African countries as well as "Africa" and "sub-Saharan Africa" were used in the search terms. Studies were included if they were population-based with a sample size > 1000, reported presenting visual acuity (PVA) with its causes, had a high participation rate (>75%) and provided the standard WHO categories of visual acuity. We also searched reference lists of studies meeting inclusion criteria. Published studies, reported in English, French and Portuguese languages were included.

The majority of these studies have used a Rapid Assessment of Avoidable Blindness methodology. RAAB data from SSA was identified through the RAAB repository (2013-17, mostly unpublished).

The existing data from the published reviews is presented below:

Reproduced from chapter 2, Bastawrous et al, Blindness and visual impairment due to age-related cataract in sub-Saharan Africa: a systematic review of recent population-based studies. *Br J Ophthalmol*. 2013 Oct;97(10):1237-43.

Table 1 Population-based studies from sub-Saharan Africa with data on blindness and age-related cataract

Country	Level	Year published	Sampling method	Sampling within cluster	Sample size (*number examined*)	Response rate (%)	Age (years)	References
Botswana	National	2009	CRS	Compact segment sampling	2127	79.9	≥50	9
Burundi	Provincial	2012	CRS	Compact segment sampling	3684	97	≥50	22
Cameroon	Limbe	2007	CRS	Compact segment sampling	2215	92.3	≥40	10
Cameroon	Muyuku	2006	CRS	Random walk	1787	89.3	≥40	11
Eritrea	National	2011	CRS	Compact segment sampling	3163	95.9	≥50	12
Ethiopia	National	2007	CRS	Random walk	25 650	85.4	All	13
Gambia	National	2000	CRS	Compact segment sampling	13 046	92	≥5	14
Ghana	City	2012	CRS	House to house census	5603	82.3	≥40	38
Guinea	District, Bioko	2002	CRS	Household cluster sampling	3218	NS	All	15
Kenya	District, Nakuru	2007	CRS	Compact segment sampling	3503	92.6	≥50	16
Malawi	District	2011	CRS	Compact segment sampling	3430	95.7	≥50	17
Mali	Subnational	2008	CRS	Compact segment sampling	2438	NS	≥50	39
Nigeria	National	2009	CRS	Random walk	13 599	89.9	≥40	18
Rwanda	Western province	2007	CRS	Compact segment sampling	2206	98	≥50	19
South Sudan	District	2006	CRS	Random walk	2499	84.6	≥5	40
Tanzania (Kilimanjaro)	Regional	2010	CRS	Random walk	3436	95.5	≥50	20
Tanzania (Zanzibar)	Island	2007	CRS	Compact segment sampling	3160	98.8	≥50	21
Uganda	15 neighbouring villages	2002	CRS	NS	4076	98.9	≥13	41

CRS, cluster random sampling; NS, not stated.

Reproduced from chapter 3, Bastawrous et al. Posterior segment eye disease in sub-Saharan Africa: review of recent population-based studies. *Trop Med Int Health*. 2014 May;19(5):600-9.

Country	Level	Year published	Sample size *(number examined)*	Response rate (%)	Age (years)	Primary cause of blindness	Secondary cause of blindness	Equipment used for diagnosis	References
Burundi	Provincial	2012	3684	97	≥50	Cataract (55%)	PSED (37%)	Not stated	Kandeke *et al.* (2012)
Cameroon	Limbe	2007	2215	92.3	≥40	Cataract (62%)	PSED (25%)	Direct ophthalmoscope	(Oye and Kuper (2007)
Cameroon	Muyuka	2006	1787	89.3	≥40	PSED (29%)	Cataract (21%)	Direct ophthalmoscope	Oye *et al.* (2006)
Eritrea	National	2011	3163	95.9	≥50	Cataract (55%)	Glaucoma (15%)	Portable slit lamp	Muller *et al.* (2011)
Ethiopia	National	2007	25650	85.4	All	Cataract (50%)	Trachoma (8%)	Direct ophthalmoscope	Berhane *et al.* (2007)
Ghana	City	2012	5603	82.3	≥40	Cataract (44%)	Glaucoma (22%)	Slit lamp/fundus camera	Budenz *et al.* (2012)
Guinea	District, Bioko	2002	3218	NS	All	Cataract (61%)	Macular Affection (21%)	Slit lamp	Moser *et al.* (2002)
Kenya	District, Nakuru (RAAB)	2007	3503	92.6	≥50	Cataract (42%)	PSED (30%)	Direct ophthalmoscope	Mathenge *et al.* (2007)
Kenya	District, Nakuru	2012	4414	88.1	≥50	Cataract (45%)	PSED (32%)	Slit lamp/fundus camera	Mathenge *et al.* (2012)
Malawi	District	2011	3430	95.7	≥50	Cataract (48%)	Glaucoma (16%)	Direct ophthalmoscope	Kalua *et al.* (2011)
Nigeria	National	2009	13599	89.9	≥40	Cataract (43%)	Glaucoma (17%)	Slit lamp/fundus camera	Abdull *et al.* (2009)
Nigeria	Local Government Area	2008	2424	93.6%	≥50	Cataract (46%)	Surgical complications (20%)	Direct ophthalmoscope	Rabiu (2008)
Rwanda	Western province	2007	2206	98	≥50	Cataract (65%)	PSED (20%)	Direct ophthalmoscope	Mathenge *et al.* (2007)
South Sudan	District	2006	2499	84.6	≥5	Cataract (41%)	Trachoma (35%)	Torch	Ngondi *et al.* (2006)
Tanzania (Kilimanjaro)	Regional	2010	3436	95.5	≥50	Cataract (51%)	PSED (36%)	Direct ophthalmoscope	Habiyakire *et al.* (2010)
Tanzania (Zanzibar)	Island	2007	3160	98.8	≥50	Cataract (67%)	PSED (25%)	Direct ophthalmoscope	Kikira (2007)
Uganda	15 neighbouring villages	2002	4076	98.9	≥13	Glaucoma (39%)	Cataract (23%)	Direct ophthalmoscope	Mbulaiteye *et al.* (2002)

NS, Not stated. RAAB, rapid assessment of avoidable blindness, PSED, posterior segment eye disease.
All studies were cross-sectional, population-based studies, which used cluster random sampling.

Table. Recent prevalence studies of blindness and visual impairment in sub-Saharan Africa taken from the RAAB Repository [http://raabdata.info/]

Country	**Level**	**Year undertaken**	**Sample size *(number examined)***	**Response Rate (%)**	**Age (years)**	**Primary cause of blindness**	**Secondary cause of blindness**	**Ref**
Madagascar	National	2015[+]	n/a	n/a	≥50	n/a	n/a	*
Rwanda	Regional	2015[+]	n/a	n/a	≥50	n/a	n/a	*
DR Congo	District, Ituri	2015	3796	93.8	≥50	Cataract (72%)	PSED (19%)	*
Botswana	National	2015	3549	93.3	≥50	Cataract (42%)	PSED (29%)	*
Uganda	State, Karamoja	2015	3850	96.8	≥50	Cataract (44%)	Trachoma (26%)	*
Uganda	District, Hoima	2013	3862	99.1	≥50	Cataract (49%)	PSED (32%)	*
Burundi	States, Ngozi and Kayanza	2012	3879	95.0	All	Cataract (55%)	PSED (38%)	*

*Unpublished data, [+]Studies completed but no data available yet

This table shows the recent studies of blindness and VI from SSA from the RAAB repository. It identified 7 new RAAB studies, conducted in SSA. Cause of blindness and VI was presented for 5 out of the 7 studies. Among these, cataract was consistently the leading cause of blindness, and PSED was the second cause in four of the five studies (making up 19-38% of blindness). Only in the survey in Uganda was trachoma the second leading cause of blindness after cataract.

Two further population based surveys of VI were identified, that did not use the RAAB methodology. These were a small survey conducted in Ghana and the national survey of blindness in Nigeria.

The survey in Ghana assessing the prevalence and causes of visual impairment and blindness among cocoa farmers, the sample size was too small to report on causes of

blindness, however the leading causes of visual impairment were cataract (38.8%), refractive errors (36.2%) and PSED (12.9%). (1)

The Nigeria National Blindness Survey, a comprehensive prevalence study (n=13,591 adults 40 years+) provides detailed information on the prevalence and causes of blindness and visual impairment. The leading causes of blindness were cataract (43.0%), glaucoma (16.7%) and uncorrected aphakia (8.4%). The leading causes of visual impairment were refractive error (61.6%) and cataract (22.1%) with PSED responsible for 25.7% and 7.1% of blindness and VI respectively.(2)

The prevalence of cataract (including those that were not visually significant) was 19.8% (95% CI: 7.9-21.7) increasing with age, and was higher in females and those not literate.(3) The age-adjusted prevalence of diabetes amongst the study population was 3.3% (95%CI 2.5-4.3); with 48% being unaware of their diabetes status at diagnosis. Digital retinal photography was conducted in participants with a presenting visual acuity of less than 6/12, of whom 52 were persons with diabetes. Lens opacity prevented gradable images in eights participants. 9/44 (20.5%) of the remaining participants had evidence of diabetic retinopathy. Persons with diabetes had three times greater odds of blindness and over 10% of people with diabetes aged ≥40 years had sight-threatening DR.(4)

The prevalence of glaucoma in the study sample was 5.02 % (95 % CI 4.60-5.47). with only 5.6 % (38/682) of participants with glaucoma being aware of their diagnosis at examination. 20% of participants with glaucoma were blind.(5)

In addition, the results from the Nakuru Posterior Segment Eye Disease survey (which forms the baseline of the current study) were published in this time period. These are presented in chapter 4.

Conclusion

Although further RAABs studies have been complete since the reviews were undertaken, no data from these has yet been published in the peer-reviewed literature. The most significant body of new data comes from the Nigeria National Survey, a West African population representing nearly one quarter of all sub-Saharan African. This comprehensive survey is consistent with findings from other countries in the region.

The primary conclusions of these two reviews still stand:

> Cataract is currently the most common cause of blindness and VI in SSA. Efforts to reduce the burden of blindness and VI due to cataract should incorporate high-volume, high-quality, affordable cataract surgery that greatly improves the CSR and CSC in such populations. This can be achieved by the implementation of well-run, cost-effective, and sustainable cataract units at the district level. Wide variation in the prevalence of cataract blindness has been shown in this review, and although this may be due to disparities in eye care programme delivery, it may also reflect inter-population differences in cataract incidence. The fundamental problems highlighted by this review are that currently too few cataract surgeries are being performed and there are too many poor outcomes. An open and urgent appraisal of positive successes throughout SSA should be

performed and shared.(6)

And,

Many studies worldwide have collected cross sectional survey data on PSED prevalence; however few studies have data on incident PSED with no SSA based eye disease cohort studies to date. The best estimates of incidence for Africa are therefore extrapolated from studies conducted elsewhere in the world. Furthermore, investigating PSED in Africa offers a new perspective on account of the different exposures and genetic make-up of these populations compared to those studied thus far, which may reveal new insights into the cause and natural history of these diseases.

Large, community-based cross-sectional and cohort studies are needed to estimate prevalence of disease, risk factors for disease, as well as incidence and progression across Africa. Inferring data from high-income countries undermines efforts to establish studies in LMIC, which will guide the effective use of minimal existing resources to deal with the growing burden of NCDs. Evidence for effectiveness and economics of screening and treatment of PSED in low resource settings is vital for health service planners.(7)

1. Boadi-Kusi SB, Hansraj R, Mashige KP, Osafo-Kwaako A, Ilechie AA, Abokyi S. Prevalence and Causes of Visual Impairment and Blindness among Cocoa Farmers in Ghana. Ophthalmic Epidemiol. 2017;24(1):17-23.
2. Rabiu MM, Kyari F, Ezelum C, Elhassan E, Sanda S, Murthy GV, et al. Review of the publications of the Nigeria national blindness survey: methodology, prevalence, causes of blindness and visual impairment and outcome of cataract surgery. Annals of African medicine. 2012;11(3):125-30.
3. Mahdi AM, Rabiu M, Gilbert C, Sivasubramaniam S, Murthy GV, Ezelum C, et al. Prevalence and risk factors for lens opacities in Nigeria: results of the national blindness and low vision survey. Invest Ophthalmol Vis Sci. 2014;55(4):2642-51.
4. Kyari F, Tafida A, Sivasubramaniam S, Murthy GV, Peto T, Gilbert CE, et al. Prevalence and risk factors for diabetes and diabetic retinopathy: results from the Nigeria national blindness and visual impairment survey. BMC Public Health. 2014;14:1299.
5. Kyari F, Entekume G, Rabiu M, Spry P, Wormald R, Nolan W, et al. A Population-based survey of the prevalence and types of glaucoma in Nigeria: results from the Nigeria National Blindness and Visual Impairment Survey. BMC Ophthalmol. 2015;15:176.
6. Bastawrous A, Dean WH, Sherwin JC. Blindness and visual impairment due to age-related cataract in sub-Saharan Africa: a systematic review of recent population-based studies. Br J Ophthalmol. 2013;97(10):1237-43.
7. Bastawrous A, Burgess PI, Mahdi AM, Kyari F, Burton MJ, Kuper H. Posterior segment eye disease in sub-Saharan Africa: review of recent population-based studies. Trop Med Int Health. 2014;19(5):600-9.

Chapter 4. Summary of baseline findings and rationale for a cohort

It is apparent that PSED is emerging as an important cause of blindness and VI in Africa. Consequently, a survey was planned in Nakuru in order to investigate the prevalence and causes of PSED in an elderly population. This was undertaken as the thesis for Dr Mathenge at LSHTM. (1-4) The methods and results are described here in brief.

Methods [taken from Mathenge W, Bastawrous A, Foster A, Kuper H. The Nakuru Posterior Segment Eye Disease Study: Methods and Prevalence of Blindness and Visual Impairment in Nakuru, Kenya. *Ophthalmology.* 119(10); 2033-9. (2)]

In 2007/8, 4,381 participants' aged ≥50 years were recruited in a population-based survey in Nakuru, Kenya. (2) These participants form the baseline population of the 6-year follow-up.

Sampling

Recent census data for Kenya were not available (5), and therefore election role lists that were renewed in 2006 in preparation for the 2007 general elections were used as the sampling frame for this survey. The population size was updated for the year 2007 using a population growth rate of 2.7% per year (6). 100 clusters were selected with a probability proportional to the size of the population. A cluster was defined as the area served by the polling station.

Households were selected within clusters using a modified compact segment sampling method (7). Each cluster was divided into segments; so that each segment

included approximately 50 people aged ≥ 50 years. For instance, if a cluster included 200 people aged ≥ 50 years then it was divided into four segments. One of the segments was chosen at random by drawing lots and all households in the segment were sequentially sampled, until 50 people aged ≥ 50 years were identified. An eligible individual was defined as someone aged ≥ 50 years living in the household for at least three months in the previous year. Age was determined using the subject's testimony, national identity cards and a calendar of historic events. If the segment did not include 50 people aged ≥ 50 years then another segment was chosen at random and sampling continued. If after enumerating individual number 49 the next household had more than one person aged ≥50 all were enumerated and invited for examination.

Examination: All participants underwent comprehensive ophthalmic and general examinations including retinal photographs detailed in the annex and repeated here:

Suitable predetermined examination sites were selected on the recommendation of the village leader with close proximity for access to the cluster and electricity supply (mains or generator) for the equipment.

The examination team was led by ophthalmologist (Wanjiku Mathenge), who examined every participant in the study and included two nurses delivering questionnaires, two fully trained ophthalmic nurses undertook visual acuity testing and autorefraction. A trained visual field technician performed field tests, an ophthalmic clinical officer took fundus photographs and a further nurse took weight,

height, blood pressure and blood tests. The team also included an office manager and two data entry clerks.

Visual Acuity (VA): The presenting visual acuity was defined as the number of letters read correctly without glasses if the participant did not have glasses or with glasses if they had them. Testing was done by an ophthalmic nurse with an assistant. Each eye was tested separately at 4 meters using a reduced logarithm of the Minimal Angle of Resolution (LogMAR) tumbling 'E' chart (8) in a well illuminated area. If the subject's vision was too poor to read any letters on the chart at four meters, then the subject was tested at 1 meter, then as follows:

- Counting Fingers (CF) - Ability to count fingers at 1m, 2m or 3m distance.
- Hand Motion (HM) - Ability to distinguish if a hand is moving or not in front of the patient's face,
- Light Perception (LP) - Ability to perceive any light and
- No Light Perception (NLP) - Inability to see any light or Total blindness.

Those who did not read 24 letters (VA<6/12) at 4m were scheduled for correction and to undergo a repeat VA measurement with the correction in place unless the vision was worse than CF in which case no correction was undertaken.

Details on diagnosis of cause and disease definition are available in chapters 6-11

Summary of main results

Table. Summary of Nakuru Cohort, baseline findings

Condition	Sub-Categories	Definition		Number of Participants	Prevalence
		LogMAR Letters	*Snellen Equivelant*		*(%, 95%CI)*
Visual Impairment	Blindness	0.1	<3/60	71	1.6 (1.2 – 2.1)
	Severe VI	2	<6/60-3/60	18	0.4 (0.3 – 0.7))
	Moderate VI	3-18	<6/18-6/60	356	8.1 (7.2 – 9.2)
	Mild VI	19-23	<6/12-6/18	224	5.1 (4.3 – 6.1)
Cataract	Any vision	-	-	1,944	44.5 (43.1-46.0)
	Blindness	0.1	<3/60	63/1,944	3.2 (2.5-4.1)
	Low Vision	2-23	<6/12-3/60	506/1,944	26.0 (24.1-28.0)
Refractive Error	-	PVA <6/12 in the better eye improving to 6/12 or better after correction		346	7.4 (6.5-8.4)
Glaucoma	Definite Glaucoma	ISGEO		203	4.6 (3.9 – 5.5)
	Suspect Glaucoma			245	5.6 (4.9 – 6.4)
Diabetic Retinopathy	Any DR	As below		70	35.9 (29.7-42.6)
	Mild NPDR	Based on: Intraretinal haemorrhages, Microaneurysms venous beading Prominent IRMA and signs of PDR		20	10.3 (6.9 - 15.0)
	Moderate NPDR			24	11.8 (7.6 - 17.9)
	Severe NPDR			9	5.1 (2.9 – 9.0)
	PDR	Neovascularisation Vitreous/pre-retinal haemorrhage		17	8.7 (5.7 – 13.1)
Age-Related Macular Degeneration	Any AMD	-		489	12.6 (11.5 – 13.8)
	Early	Based on: Pigment, drusen		442	11.4 (10.3 – 12.7)
	Late	GA, CNVM		47	1.3 (1.1 – 1.6)

CI: Confidence Interval, VI: Visual Impairment, DR: Diabetic Retinopathy, NPDR: Non-Proliferative Diabetic Retinopathy, PDR: Proliferative Diabetic Retinopathy, IRMA: Intraretinal Microvascular Anomalies, AMD: Age-Related Macular Degeneration, GA: Geographic Atrophy, CNVM: Choroidal Neovascular Membrane, PVA: Presenting Visual Acuity

44.5% and 26.9% of the baseline population had evidence of cataract and PSED respectively. Of the 71 blind individuals, 32 (45.1%) were cataract blind and 23 (32.3%) were blind from PSED. Among those with PSED and blindness the causes were: glaucoma 34.7%, DR 13.0%, AMD 30.4% and other PSED 21.7%.

PSED were responsible for 11.1% of all VI in Nakuru (Glaucoma 18.9%, diabetic retinopathy 18.9%, AMD 37.8% and Other PSED 24.3%).

The following manuscripts have been published on the baseline data and are included in the annex:

The Nakuru posterior segment eye disease study: methods and prevalence of blindness and visual impairment in Nakuru, Kenya.
Mathenge W, **Bastawrous A**, Foster A, Kuper H.
Ophthalmology. 2012 Oct;119(10):2033-9. doi: 10.1016/j.ophtha.2012.04.019. Epub 2012 Jun 19.

Prevalence of age-related macular degeneration in Nakuru, Kenya: a cross-sectional population-based study.
Mathenge W, **Bastawrous A**, Peto T, Leung I, Foster A, Kuper H.
PLoS Med. 2013;10(2):e1001393. doi: 10.1371/journal.pmed.1001393. Epub 2013 Feb 19.

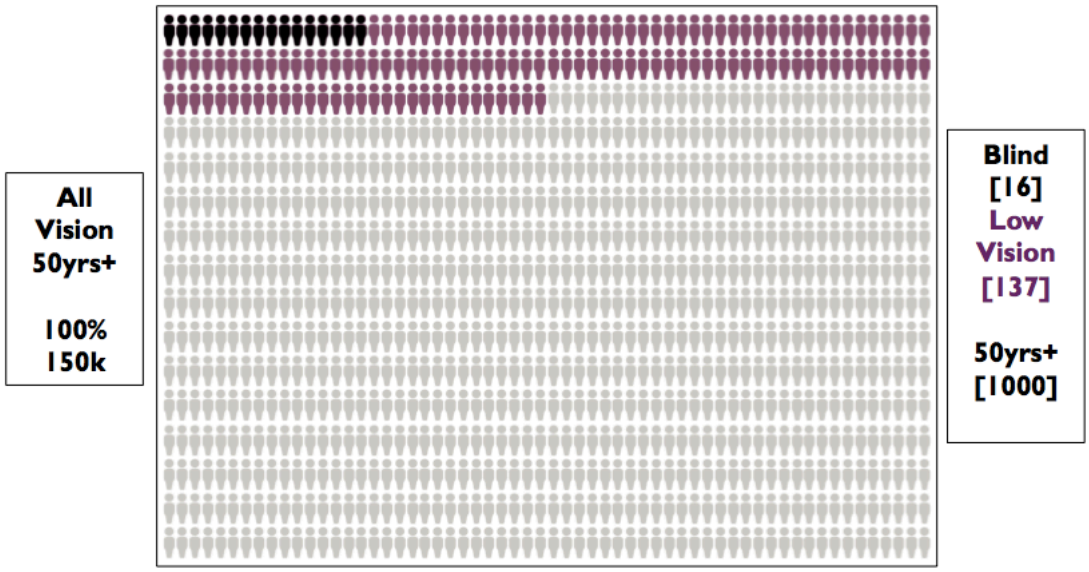
Prevalence and predictors of refractive error and spectacle coverage in Nakuru, Kenya: a cross-sectional, population-based study.
Bastawrous A, Mathenge W, Foster A, Kuper H.
Int Ophthalmol. 2013 Oct;33(5):541-8. doi: 10.1007/s10792-013-9742-6. Epub 2013 Feb 26.

Prevalence and correlates of diabetic retinopathy in a population-based survey of older people in Nakuru, Kenya.
Mathenge W, **Bastawrous A**, Peto T, Leung I, Yorston D, Foster A, Kuper H.
Ophthalmic Epidemiol. 2014 Jun;21(3):169-77. doi: 10.3109/09286586.2014.903982. Epub 2014 Apr 23.

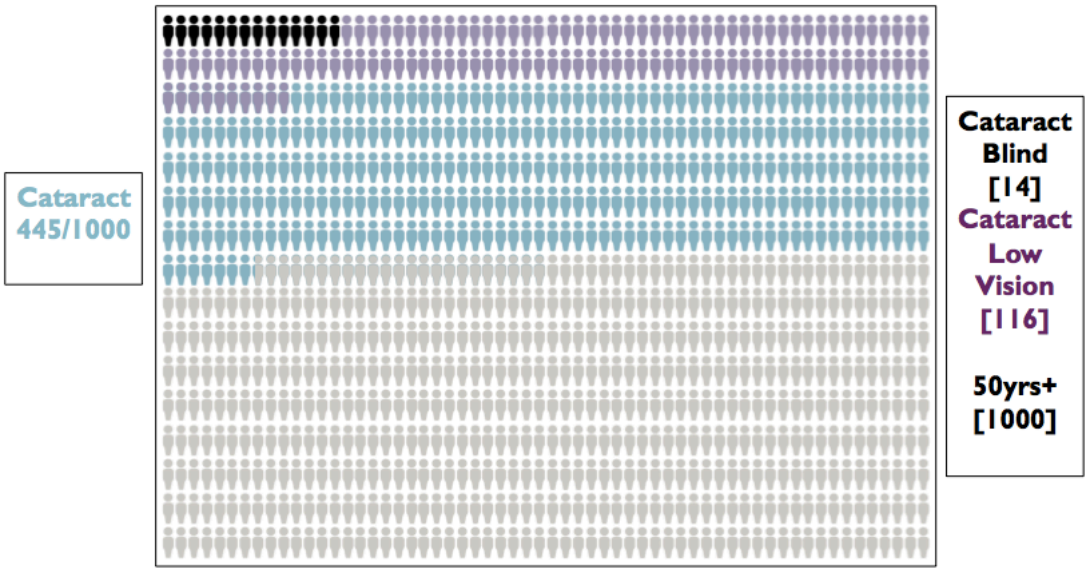
The following diagrams summarise the findings in a per 1000 of population viewpoint. Note the estimated population of adults aged 50 years and older in Kenya in 2015 was 4.3 million and 150,000 in Nakuru County.

Figures of Baseline Data

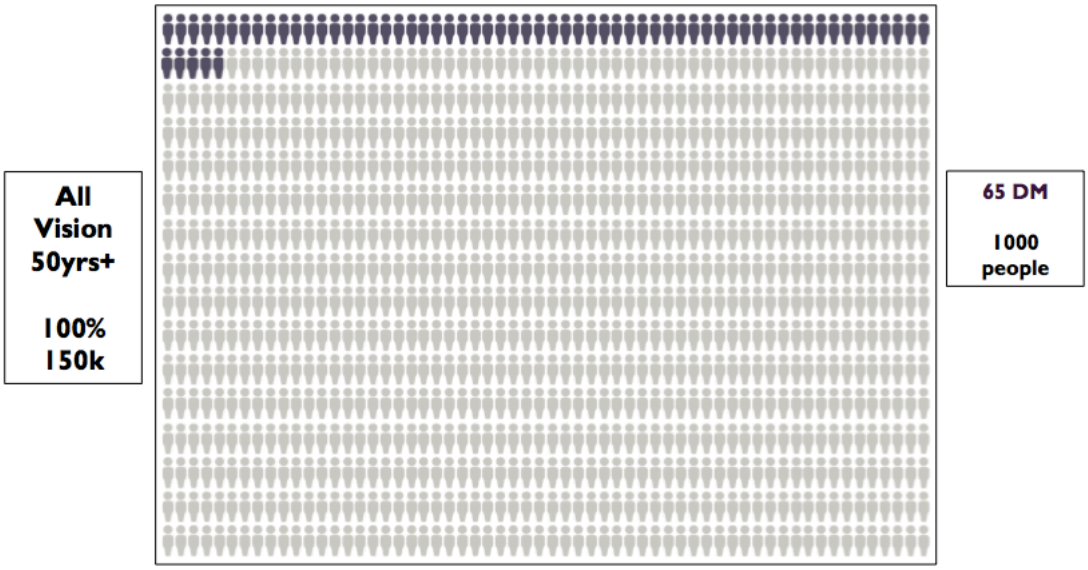
Blindness and Visual Impairment in Nakuru Kenya: There are an estimated 150,000 adults aged 50 years and older. For every 1,000 adults, 153 are visually impaired (16 blind and 137 with low vision)



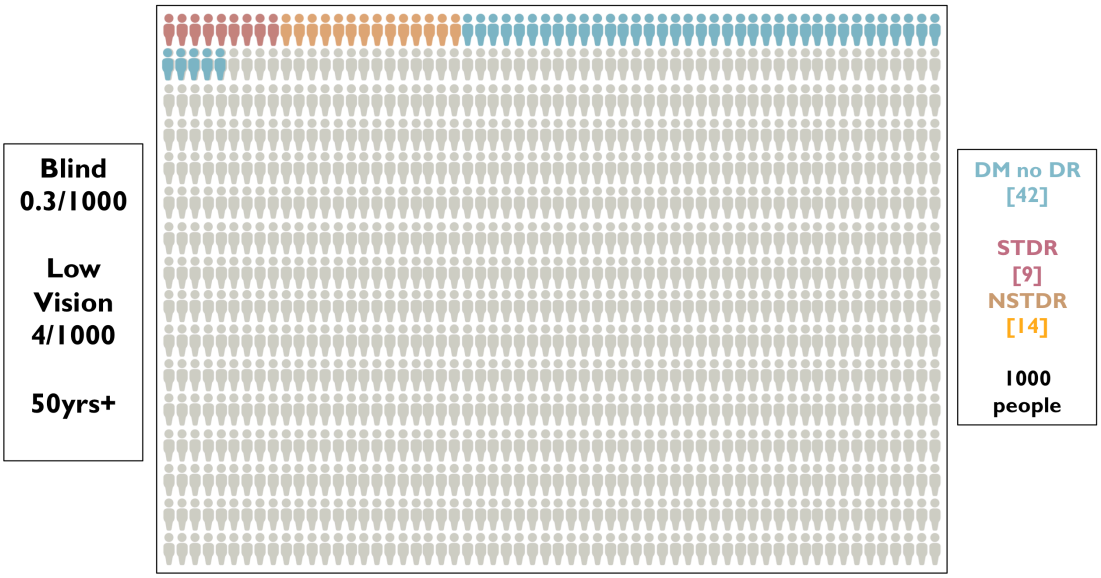
Cataract Blindness and Visual Impairment in Nakuru Kenya: For every 1,000 adults, 445 have cataract, of whom 130 are visually impaired (116 have low vision and 14 are blind).



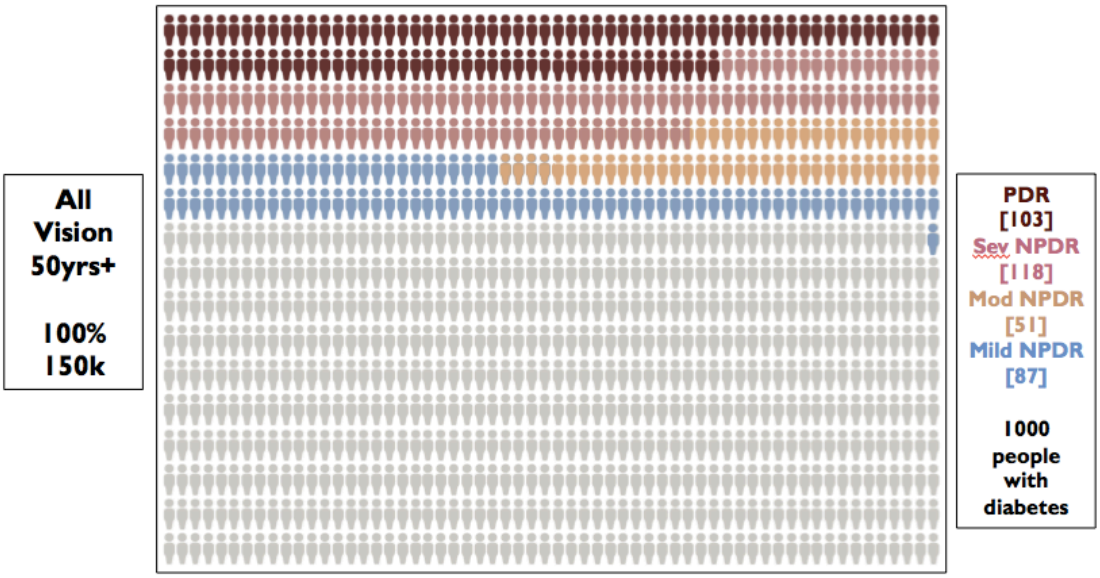
Diabetes Mellitus in Nakuru Kenya: For every 1,000 adults, 65 have diabetes mellitus



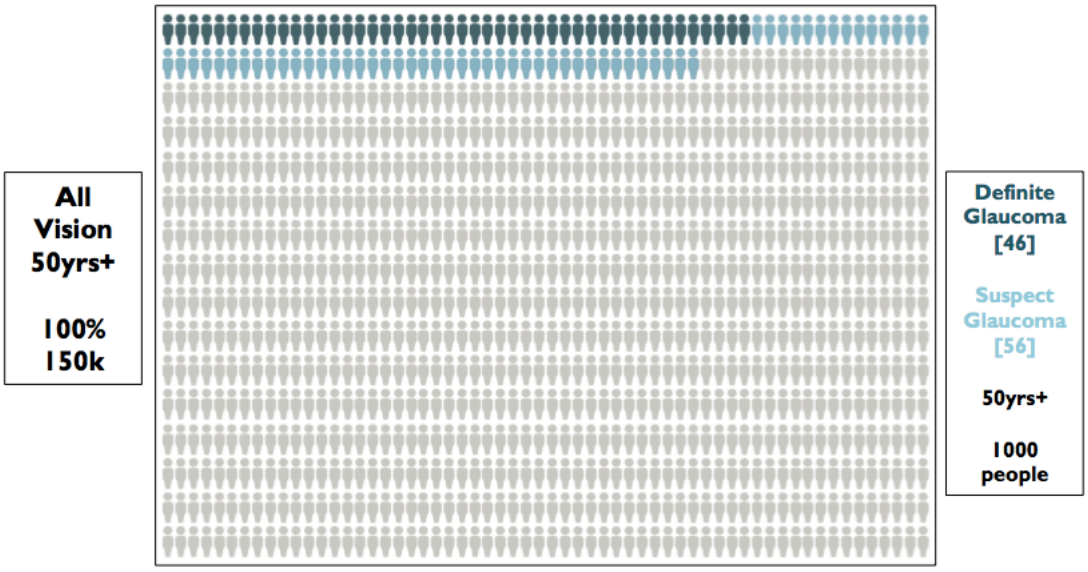
Diabetic Retinopathy amongst adults aged 50 years and over in Nakuru Kenya: For every 1,000 adults 65 have diabetes of which nine have sight-threatening diabetic retinopathy (proliferative and severe non-proliferative diabetic retinopathy) and 14 have non sight-threatening diabetic retinopathy (mild and moderate non-proliferative diabetic retinopathy). 42 adults with diabetes mellitus do not have diabetic retinopathy.



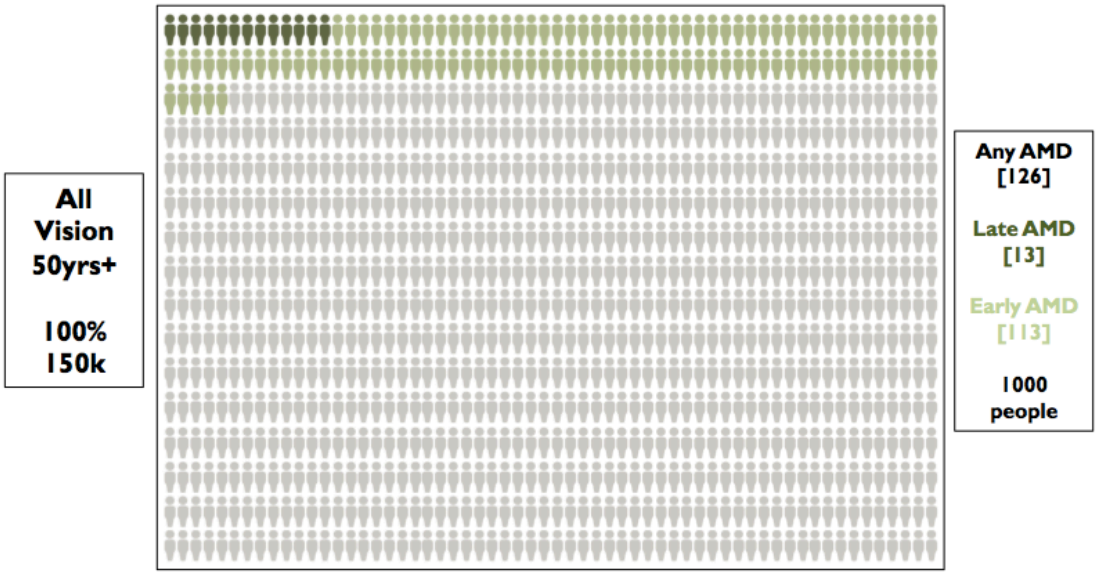
Diabetic Retinopathy amongst adults (aged 50 years and over) with diabetes in Nakuru Kenya: For every 1,000 adults with diabetes, 103 have proliferative diabetic retinopathy, 118 have severe non-proliferative diabetic retinopathy, 51 have mild non-proliferative diabetic retinopathy and 87 have mild non-proliferative diabetic retinopathy.



Glaucoma in Nakuru Kenya: For every 1,000 adults, 46 have definite glaucoma and 56 have suspect glaucoma based on ISGEO definitions.(9)



Age related macular degeneration (AMD) in Nakuru Kenya: For every 1,000 adults, 126 have AMD, of whom 13 have late AMD and 113 have early AMD,



Definition of AMD based on the modified version of the International Classification and grading system for age-related maculopathy and age-related macular degeneration. Early = drusen and /or pigmentation, Late = geographic atrophy and / or neovascular membrane

Discussion

Key findings (2-4, 10)

Prevalence of Visual Impairment and Blindness (2)

The results confirm that prevalence of blindness is relatively low as suggested by recent RAAB surveys (10, 11) and that it may be declining compared to earlier surveys.(12)

Prevalence of age related macular degeneration (3)

Despite the long held belief that AMD is not a public health concern in Africa, this study provides evidence that not only is AMD as prevalent as in some other world regions (12.6% in this population) but it is also an important problem contributing to both visual impairment and blindness in Africa. 9.9% of blindness in this survey was attributable to AMD. The Nigeria Survey used similar methodology including a population-based approach and fundus photographs, however, retinal imaging was only performed in individuals with a visual acuity of ≤6/12 (17); in the present study, 75.1% of individuals identified as having AMD had an acuity of 6/12 or greater.

Prevalence of Diabetes and Diabetic Retinopathy (4)

The baseline survey found a 6.5% prevalence of diabetes. A The overall prevalence of any DR among the 195 definite patients with diabetes with retinal images in the study population was 35.9% (95% CI: 29.7-42.6). The most common grade of DR was mild/moderate NPDR (22.1%, 16.1-29.4), while severe NPDR or PDR were less frequent (13.9%, 10.0-18.8).

Prevalence of Cataract

Cataract was widely prevalent in this study population with 1,944 participants having evidence of a lens opacity on dilated slit lamp examination, 44.5% (95% CI 43.1% - 46.0%). Of those, 506, 11.6% (95% CI 10.7% - 12.6%) had vision between 6/18 and 3/60 (low vision) and 63, 1.4% (95% CI 1.1% - 1.8%) were blind. Of the 71 blind in the study, 63 were known to have cataract.

Prevalence of Glaucoma

It was not possible to accurately estimate glaucoma from the baseline data. The ISGEO classification (9) was used, however visual field data was unreliable and for logistical reasons, gonioscopy was not performed, meaning there was no direct visualisation of the angle and a true ISGEO classification of glaucoma was not possible. A description of the distribution of features associated with glaucoma (VA, intraocular pressure, vertical cup to disc ratio, angle OCT) are described in the data chapter.

Strengths of the baseline survey

The survey design for the baseline study was strong using a population-based sample with a high response rate (88%) and large sample size (comparable to other studies worldwide) enabling estimated with narrow confidence intervals. A single examination team throughout reduced measurement bias and comprehensive ophthalmic assessment methods and equipment were used providing high quality data on the eye health status of study participants, including digital retinal photography independently graded at a certified reading center enabled comparison with similar cross-sectional population-based studies from other parts of the world. Detailed risk factor analysis was undertaken, again using reference standard methods.

Limitations of the baseline survey

The sampling frame ideally would have used the most recent census data, which was several years out of date, thus the electoral role was used. It was felt this was likely to be a fair reflection of the population. Despite a high response rate there was a slight gender bias with greater response from men than women (89 vs. 86%). The use of reference standard ophthalmic equipment was a barrier to data collection as the majority of equipment was designed for more developed infrastructure (reliable electricity, dust free, stationary) it was not suitable for use across multiple temporary examination clinics (n=100) resulting in retinal camera failure. Visual Field analysis was not reliable across all study participants for which it was undertaken making any assessment of glaucoma limited.

Overall

This study was undertaken in a challenging setting with the backdrop of a complex political situation. The quality of data despite all the challenges make this one of the most comprehensive prevalence studies of eye disease ever completed in Africa. An absence of incidence data from the region remains one of the main unexplored questions. This study therefore provides a solid foundation for a cohort study.

Sample Size Implications

4,381 participants were examined at baseline across 100 clusters. A pilot follow up retraced 408 participants from 10 of the 100 clusters at a mean of 1.5 years from completion of the baseline study.

Estimated follow-up at 6 years is based on an assumption of a constant rate of loss per year (constant proportion of those still in follow-up who are lost each year)

Assuming that the pilot followed 438 individuals, and saw 408 at 1.5 years

- We estimate that 2/3 of the 30 lost were lost in the first year (20/438= 4.6%)
- If 4.6% are lost per year for each of the 6 years, then the number at follow-up would be 4381*(1-0.**046**)^6 = 3,303.
- This means follow-up of 3468/4381=75.4%
- Which equates to a 4.2% loss per year.

Due to anticipated displacement due to the post-election violence in the study region Follow up is estimated at a conservative 8% loss per year ([4381*(1-**0.08**)^6] equating to an approximate cumulative follow-up of 61%; n=2,656) examined at 6-year follow up. All participants included in the baseline study were invited to attend for follow-up.

The following table was a prediction of ranges of expected incidence for the key areas of interest in the cohort study based on studies of similar design.

A Design Effect (DEFF) of 1.4, to account for clustering, has been used in all the following calculations: (http://www.sph.emory.edu/~cdckms/proportionDEFF.html. Version 7.02.15)

Table. Expected 5-year cumulative incidence (based on similar studies) (18-25).

Outcome	Number free of condition at baseline "At risk"	Number free of condition at baseline examined at follow-up (assuming 65% follow-up)	Expected 5 year cumulative incidence *Lower – Upper estimates*	95% CI Precision	Actual 6 (5.6) year cumulative incidence (95%CI)
Blindness	4310	2802	0.48-0.75*	0.23-0.85% 0.41-1.22%	2.70% (1.8-3.1)
Visual Impairment	3712	2413	3.0-4.5*	2.26-3.89% 3.57-5.55%	11.9% (10.3-13.8)
AMD	3842	2497	4.75-11.25%*	3.80-5.81% 9.80-12.77%	16.4% (13.7-19.6)
Glaucoma	4180	2717	3.7-5.2%**	2.91-4.61% 4.27-6.27%	Unknown
DR	DM no DR 190	124	20-35%***	12.21-28.88% 25.54-45.48%	22.5% (11.7-38.8)

The five year cumulative incidence estimates for new cases of each disease are based on the following cohort studies: Beaver Dam Eye Study, Blue Mountain Eye Study, AREDS, Rotterdam Eye Study, PONZA study

*Based on BDES, BMES, Copenhagen and LALES
** Based on Barbados Eye Study
*** Based on BDES, BMES, Japanese Eye Study and San Luis Valley Diabetes Study

Lessons learnt from baseline for the cohort

To maximize coverage and quality of data collection at follow up, with the same barriers to data collection as baseline, various modifications to the methodology were undertaken, with the majority of procedures remaining unchanged.

Changes in methodology and rationale for this are discussed in detail in the methodology chapter. Key changes included use of a different retinal camera that would more likely survive the environment and the use of a different visual field

analyser. The lack of reliable visual field data at baseline limits the interpretation for longitudinal population changes (incidence and progression) for glaucoma.

The importance of a cohort study

The conclusion of the review of the baseline study is that this would make an appropriate foundation on which to establish a cohort study. There are several reasons why this may be a worthwhile endeavor.

Many studies worldwide (26-29) have collected cross sectional survey data on cataract and PSED prevalence; however very few have data on incident cataract or PSED with no African based eye disease cohort studies to date (bar DR from studies of persons with DM). The best estimates of incidence for Africa are therefore extrapolated from studies conducted elsewhere in the world.

Prevalence data is limited in terms of planning services for the sample population, as it does not provide information on the rate of change of conditions or the rate at which subjects might become cases that require an intervention. For example, knowing the prevalence of visually significant cataract at best defines that there is a need for more services; however defining the required services more specifically requires an estimate of the number of new cases over a period of time (usually one year).

The best estimates of incidence for Africa are therefore extrapolated from studies conducted elsewhere in the world.

Planning healthcare provision requires a good estimate of new cases (incidence) not just prevalence. An effective health service will provide treatment (curative or preventative) to its population at a rate that is equal to or greater than the number of new cases per population requiring those services. If the treatment rate is less than the incidence rate the backlog (waiting list or prevalence) will increase. The prevalence alone does not give accurate data for estimating the required level of service provision. A high prevalence indicates insufficient services however as it is a snapshot of a single time frame it does not provide a complete picture.

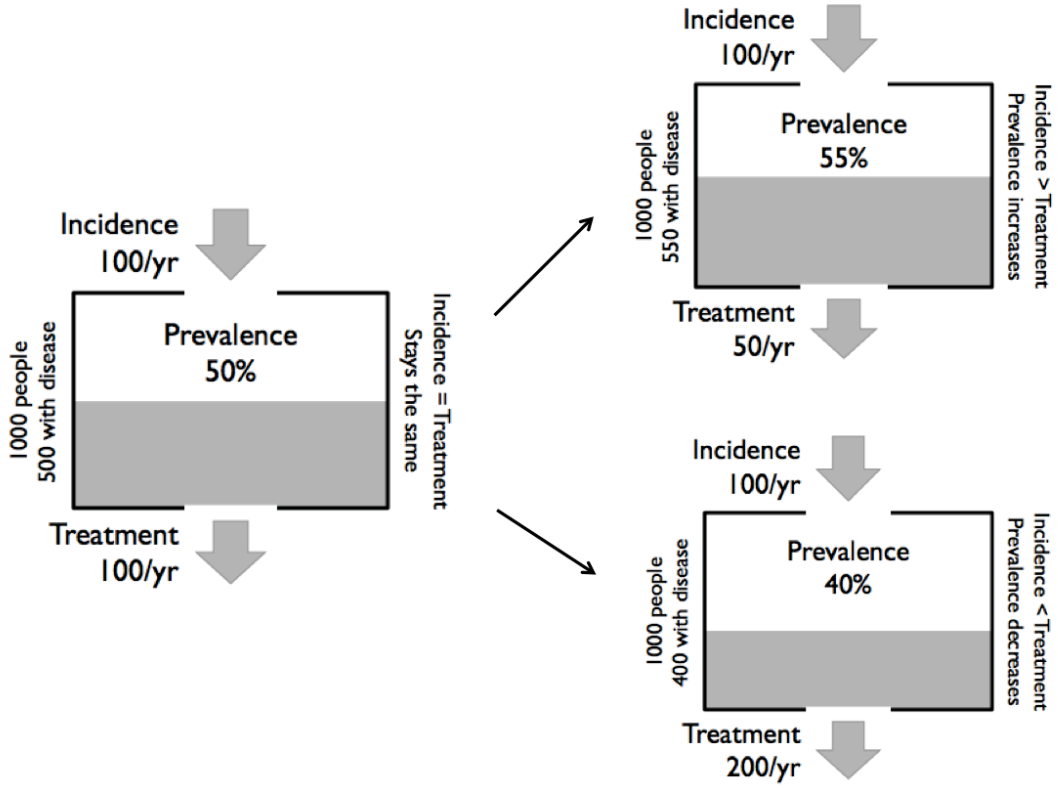
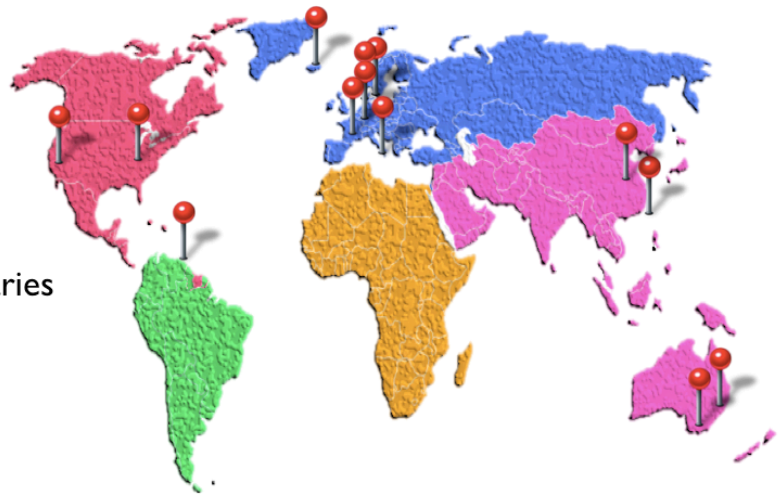


Figure. Prevalence, Incidence and the importance for planning services

Longitudinal data will also enable a greater understanding of the aetiology of diseases, their natural history and associated risk factors. This is particularly important in Africa where data is lacking and we cannot assume that the aetiology will be the same across the world, given the unique constellation of environmental and genetic conditions in Africa. As an example, there is a widespread belief that the aetiology of AMD is different in Africa to elsewhere, and that glaucoma may present more aggressively.

Major population-based cohort studies of eye disease have predominantly taken place in high-income settings.

Beaver Damn
Blue Mountains
Melbourne
Rotterdam
Dalby
Ponza
Copenhagen
Pathologies Ocularies
Hisayama
Reykjavic
LALES
Barbados
Beijing



It is assumed that incidence in Africa will most closely reflect that of the Barbados Eye Study in whom enrolled participants were of African descent. (30, 31) Other major cohort studies with comparable data to the Nakuru Cohort Study include the

Beaver Dam Eye Study, (18) Hisayama Eye Study, (19) Ponza Eye Study, (20) Beijing Eye Study, (21) the Dalby Eye Study (22), the Blue Mountain Eye Study, (23) the Melbourne Visual Impairment Study (24) and the Rotterdam Eye Study (25). These cohorts will be used for comparison with the findings from this cohort in the data chapters.

These major cohort studies are summarised in the table below:

Study	Location	Year commenced	Years of Follow up	No of participants	Age at Baseline	Reference
Beaver Dam Eye Study	USA	1988	Baseline 5 10 15	4926 3684 2764 2119	43-86	(32-34)
Blue Mountain Eye Study	Australia	1992	Baseline 5 10	3654 2335 1952	49+	(35)
Rotterdam Study	Netherlands	1990	Baseline 2 6.5 11	6418 4953 3406 2387	55+	(36, 37)
Copenhagen City Eye Study	Denmark	1986	Baseline 14	946 359	60-80	(38)
Barbados Eye Study	Barbados	1987	Baseline 4 9	4631 3427 2793	40+	(39, 40)
Pathologies Oculaires Liees a L'Age	France	1995	Baseline 3	2584 1642	60+	(41)
Melbourne Visual Impairment Project	Australia	1992	Baseline 5	5147 3271	40+	(42)
Hisayama Study	Japan	1998	Baseline 5 9	1482 961 (1401>40yrs)	40+	(19, 43)
Reykjavik Eye Study	Iceland	1996	Baseline 5	1045 846	50+	(44)
Los Angeles Latino Eye Study	USA	2000	Baseline 4	6357 4658	40+	(45)

It is therefore clear that the cohort studies on eye disease that exist focus on high income countries, and people of Caucasian ethnicity. A cohort study of eye disease conducted in SSA will therefore make an important contribution to the literature.

Aim of the study

To investigate the epidemiology of cataract and posterior segment eye disease, including diabetic retinopathy and age related macular degeneration, in Nakuru county, Kenya.

Objectives

Incidence

1. To estimate the age- and sex- specific incidence of visual impairment (VA<6/12) and blindness (VA<3/60)
2. To estimate the age- and sex- specific incidence of diabetes mellitus and diabetic retinopathy
3. To estimate the age- and sex- specific incidence of features of glaucoma
4. To estimate the age- and sex- specific incidence of age related macular degeneration

Causes & Risk Factors

5. To identify the causes and risk factors for incident visual impairment and blindness, diabetes, diabetic retinopathy, age-related macula degeneration, cataract and features of glaucoma (specifically focusing on ophthalmic, demographic, anthropometric, behavioural, and vascular risk factors)

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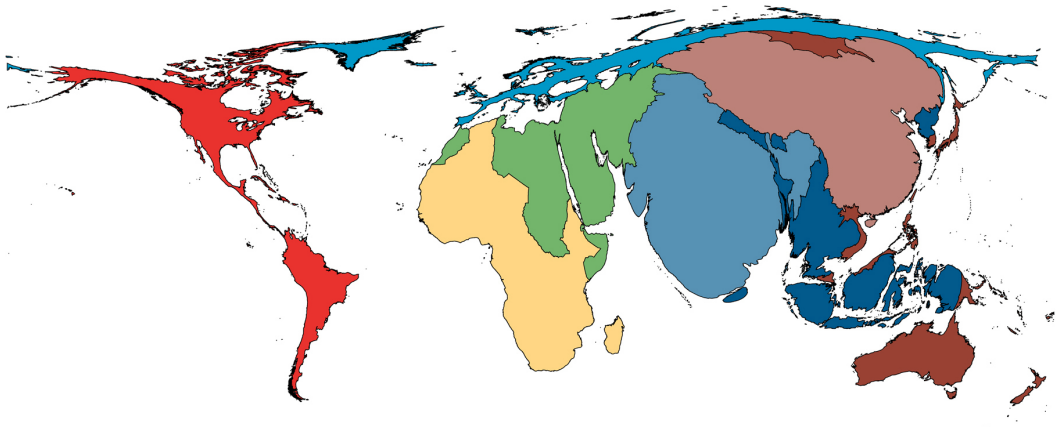
Chapter 5. The global inverse care law: a distorted map of blindness



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Student	Andrew Bastawrous
Principal Supervisor	Hannah Kuper
Thesis Title	The Nakuru Eye Disease Cohort Study

If the Research Paper has previously been published please complete Section B, if not please move to Section C

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LETTER

The global inverse care law: a distorted map of blindness

Statistical analysis can be used to interpret and give meaning to data, however, the ability to interpret large quantities of data and it's resulting statistical reporting is not always straightforward. Graphical representations such as graphs and maps are a way of translating or converting data into a visual interpretation.

Commonly used world maps are imperfect and contain distortions to allow a spherical reality to be represented in 2-dimensions. This distortion can be manipulated to produce a world map that gives each defined area (country or region) a size proportional to its population.[1]

Cartograms are used to effectively map socioeconomic data and can be effective means of mapping disease. In keeping with the phrase 'a picture equals a thousand words' cartograms can be used to analyse spatial data in an easily comprehensible style.

In 1971, Hart[2] described the, 'Inverse Care Law' as the availability of good medical care varying inversely with the need for it in the population served. Hart was describing the situation in the National Health Service in Great Britain at the time in which he practiced as both a General Practitioner and an epidemiologist.

Two recently published articles demonstrate the 'Inverse Care Law' on a global level. The prevalence of blindness worldwide in 2010[3] was reported by the WHO and verified that low- and middle-income countries, as expected, have the highest prevalence of blindness and visual impairment. In stark contrast to this, a more recent report describes the, "Number of ophthalmologists in training and practice worldwide"[4] providing global data for the number of ophthalmologists per county and demonstrates that despite a growing number in practice the gap between need and supply is widening.

The situation is also magnified within individual countries of high, middle and low-income. For example, in France, an inverse correlation was found between the number of ophthalmologists and the prevalence of low vision for subjects of similar age and socio-professional category[5] and another example is in Kenya where of the 86 practicing ophthalmologists, 43 are based in Nairobi (personal correspondence). That equates to 50% of the countries ophthalmologists serving 8% of an already underserved population.

We have developed two cartograms to depict the data from these two papers[3 4] using ESRI's ArcGIS 10 software with the Cartogram Creator. These tools apply the Gastner & Newman diffusion-based method.[6] This allowed us to create density-equalised maps based on the absolute values provided in the papers. In the maps, each of the reference areas (WHO regions and countries) is resized according to these values. Larger areas represent higher numbers and smaller areas proportionally smaller data values (see figures 1 and 2).

We believe these maps can be used to share masses of data in a visual, intuitive and comprehensible way, which will be understood by policy makers and can be used by advocates for global health.

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Competing interests None.

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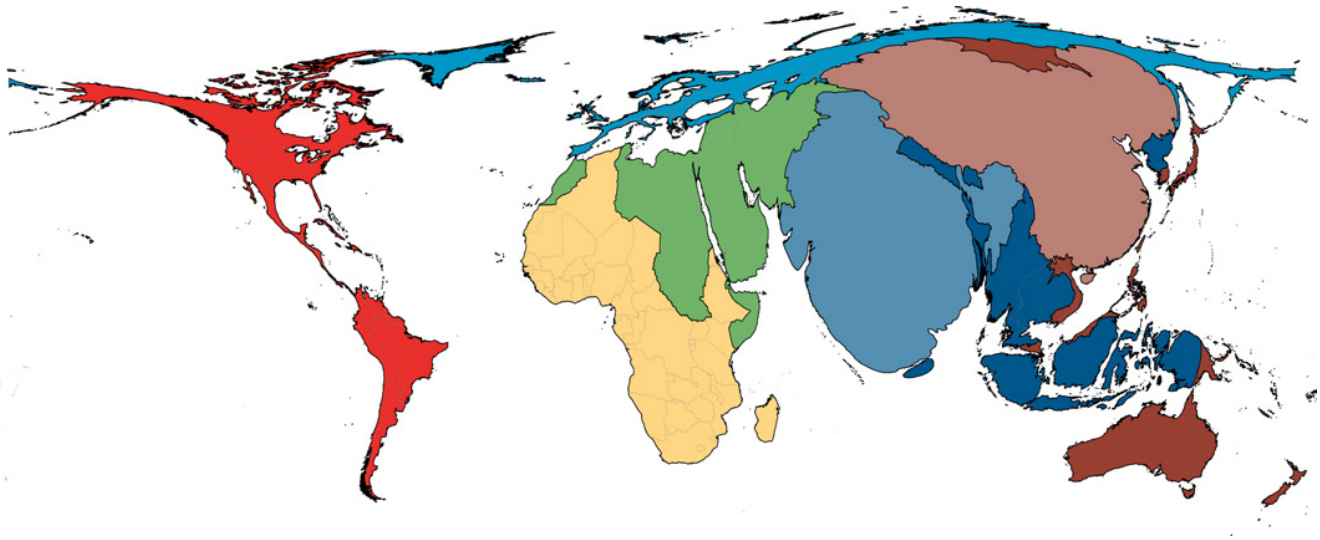

Figure 1 Cartogram showing the prevalence of blindness by WHO region (using WHO region colours).

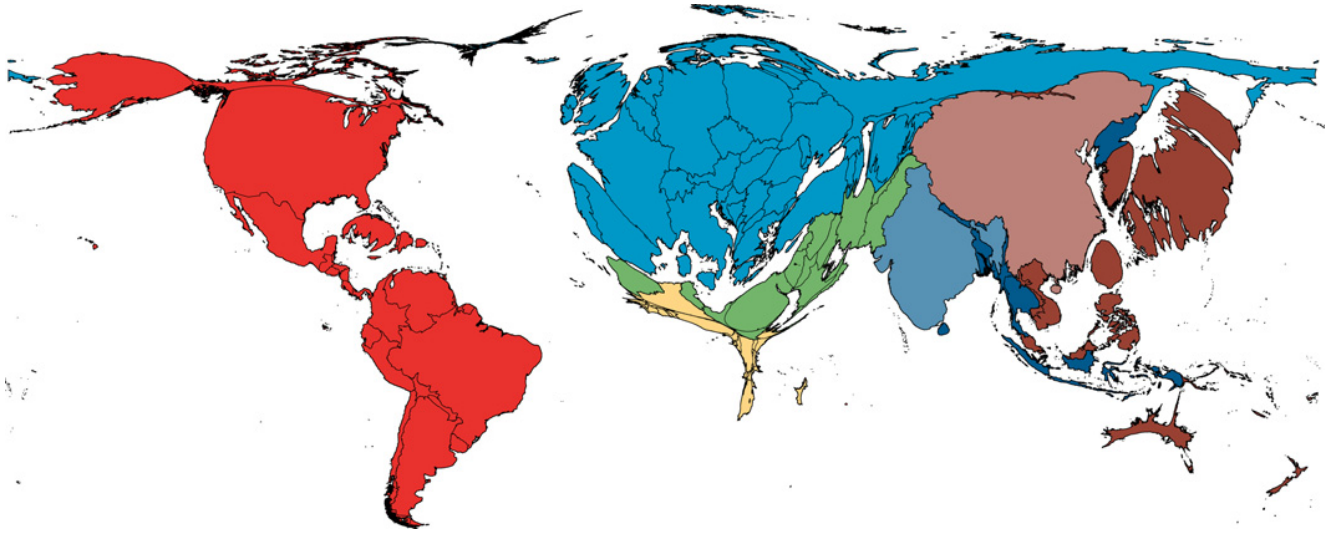

Figure 2 Cartogram showing the number of practicing ophthalmologists worldwide by country.

Bastawrous A, Hennig BD. *Br J Ophthalmol* (2012). doi:10.1136/bjophthalmol-2012-302088

The global inverse care law: a distorted map of blindness

Andrew Bastawrous and Benjamin D Hennig

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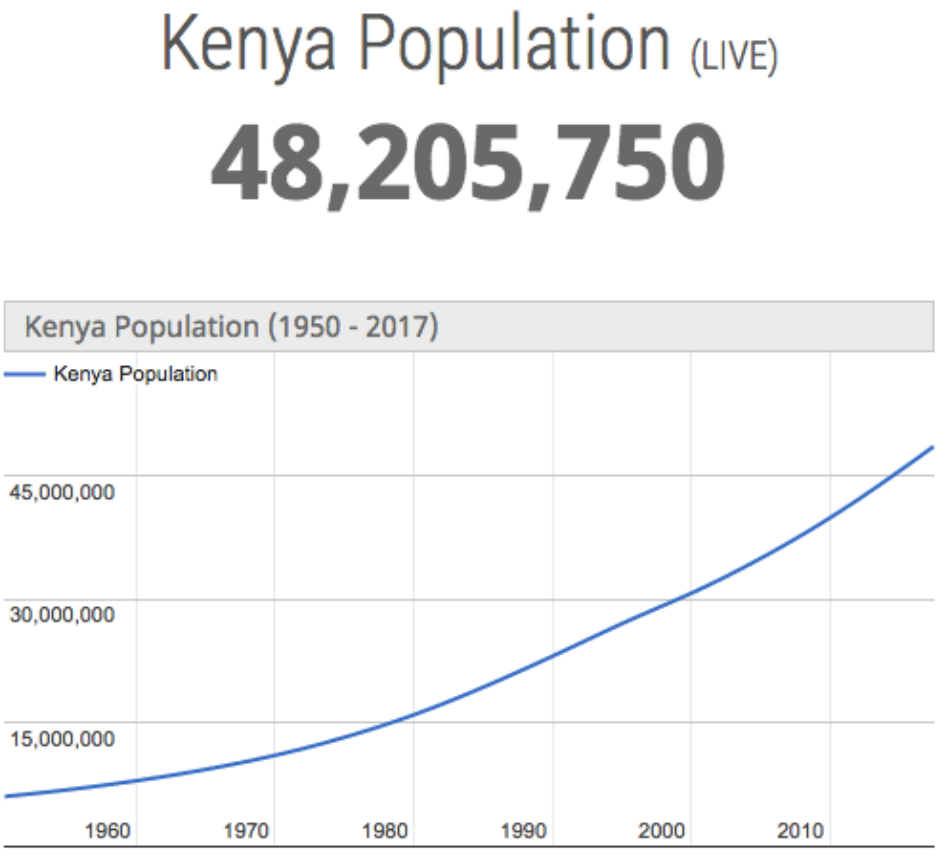
In the "The global inverse care law: a distorted map of blindness" article I discuss the disproportionate provision of services to areas with least need and inversely, areas of greatest need having the least services. (1)

The most recent population estimates in Kenya based on predicted growth by the World Bank indicate there are 48 million people

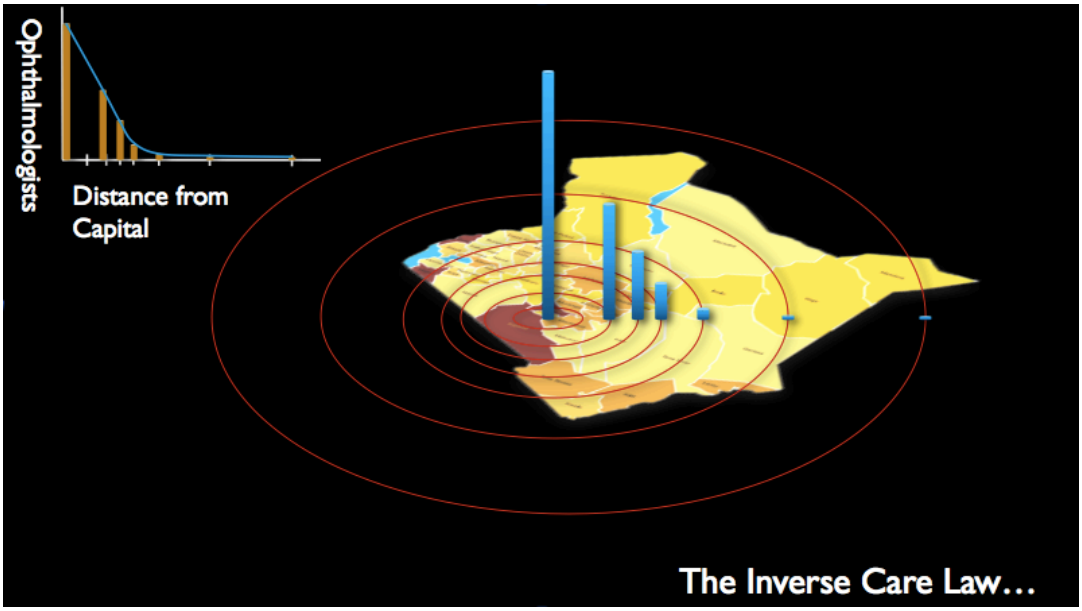
(Source: http://www.worldometers.info/world-population/kenya-population/).



This figures shows an approximate increase of ten million people since the baseline study was initiated in 2007. (2)

The number of practicing ophthalmologists has also increased by approximately 10% in this time with current estimates being there are 100 practicing ophthalmologists in Kenya, although many of them do not work in the public sector and at least 50% are based in Nairobi or its suburbs (personal communication).

Figure: Distribution of ophthalmologists throughout Kenya



In some areas of Kenya a single ophthalmologist is responsible for a population of up to three million people.

Nakuru County in Kenya, the location in which this cohort study was undertaken has a population of 1.6 million people of which approximately 150,000 are adults aged 50 years and over.

Figure: Nakuru County, Kenya (downloaded from:

https://en.wikipedia.org/wiki/Nakuru_County)

Nakuru County has one public sector eye unit in the Rift Valley Provincial General Hospital. The hospital has one ophthalmologist and two ophthalmic clinical officers, one of whom is also a cataract surgeon. The region also has a mission hospital, St Mary's Hospital in Elementatita which has an active unit served by 1.2 ophthalmic clinical officers (both cataract surgeons) and one ophthalmologist in the private sector. In total, therefore, there are 2 ophthalmologists and 3.2 ophthalmic clinical officers for the population of 1.6 million. Patients who can afford eye services frequently travel to one of the numerous options in Nairobi and occasional outreach from service providers is arranged within Nakuru County.

In conclusion, the current level of services available in Nakuru County are not able to meet the growing demand for services and those in the lowest economic groups

and rural areas are the least likely to be able to access the services that are available.

(3, 4)

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Chapter 6. The Nakuru eye disease cohort study: methodology & rationale

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Student	Andrew Bastawrous
Principal Supervisor	Hannah Kuper
Thesis Title	The Nakuru Eye Disease Cohort Study

If the Research Paper has previously been published please complete Section B, if not please move to Section C

SECTION B – Paper already published

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Bastawrous et al. BMC Ophthalmology 2014, 14:60
http://www.biomedcentral.com/1471-2415/14/60

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The Nakuru eye disease cohort study: methodology & rationale

Andrew Bastawrous[1*], Wanjiku Mathenge[3], Tunde Peto[2], Helen A Weiss[5], Hillary Rono[6], Allen Foster[1], Matthew Burton[1,2] and Hannah Kuper[1,7]

Abstract

Background: No longitudinal data from population-based studies of eye disease in sub-Saharan-Africa are available. A population-based survey was undertaken in 2007/08 to estimate the prevalence and determinants of blindness and low vision in Nakuru district, Kenya. This survey formed the baseline to a six-year prospective cohort study to estimate the incidence and progression of eye disease in this population.

Methods/Design: A nationally representative sample of persons aged 50 years and above were selected between January 2007 and November 2008 through probability proportionate to size sampling of clusters, with sampling of individuals within clusters through compact segment sampling. Selected participants underwent detailed ophthalmic examinations which included: visual acuity, autorefraction, visual fields, slit lamp assessment of the anterior and posterior segments, lens grading and fundus photography. In addition, anthropometric measures were taken and risk factors were assessed through structured interviews. Six years later (2013/2014) all subjects were invited for follow-up assessment, repeating the baseline examination methodology.

Discussion: The methodology will provide estimates of the progression of eye diseases and incidence of blindness, visual impairment, and eye diseases in an adult Kenyan population.

Keywords: Cohort study, Longitudinal, Eye disease, Africa, Kenya, Cataract, Glaucoma, Age related macular degeneration, Diabetic retinopathy, Refractive error, Incidence, Progression

Background

The most recent global estimates suggest 285 million people worldwide are visually impaired, of whom, 39 million are blind [1]. The WHO defined Africa region has 26 million people with visual impairment (VI) of whom 6 million are blind. The continent also has the greatest disparity between numbers blind and number of ophthalmologists per million people [2], and therefore the greatest need for scaling up services.

In recent years several cross-sectional surveys have been undertaken across Africa to estimate prevalence and causes of blindness [3-16]. Whilst this information has been vital in planning services where resources and provision of healthcare are limited, data on incidence and rates of progression of eye disease are needed to allow long-term planning. To date, no longitudinal, population-based studies of eye disease have been undertaken in Africa, and there have been only ten worldwide, predominantly in high-income settings (Table 1) [17-26].

The current study was undertaken in Nakuru district (now Nakuru County), which is the main district of Kenya's largest province, the Rift Valley and has a population of 1.6 million. Nakuru district is broadly representative of Kenya in terms of ethnic diversity and economic activities. In 2004, a Rapid Assessment of Avoidable Blindness (RAAB) was completed in Nakuru district, to estimate the prevalence and causes of avoidable blindness and VI in the population of those 50 years and over [7]. A subsequent more comprehensive study was planned in the same region as a consequence of this survey to estimate causes and risk factors for those with visual impairment as well as those with non-visually impairing eye disease, with a particular focus on posterior segment eye disease [6].

Fieldwork was carried out in 2007 and 2008, during the course of which 4414 participants (a response rate of

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Table 1 Population-based cohort studies of eye disease (not exhaustive)

Study	Location	Year commenced	Years of follow up	No of participants	Reference*
Beaver Dam Eye Study	USA	1988	Baseline	4926	[17]
			5	3684	
			10	2764	
			15	2119	
Blue Mountain Eye Study	Australia	1992	Baseline	3654	[18]
			5	2335	
			10	1952	
Rotterdam Study	Netherlands	1990	Baseline	6418	[19]
			2	4953	
			6.5	3406	
			11	2387	
Copenhagen City Eye Study	Denmark	1986	Baseline	946	[20]
			14	359	
Barbados Eye Study	Barbados	1987	Baseline	4631	[21]
			4	3427	
			9	2793	
Pathologies Oculaires Liees a L'Age	France	1995	Baseline	2584	[22]
			3	1642	
Melbourne Visual Impairment Project	Australia	1992	Baseline	5147	[23]
			5	3271	
Hisayama Study	Japan	1998	Baseline	1482	[24]
			5	961	
			9	(1401>40 yrs)	
Reykjavik Eye Study	Iceland	1996	Baseline	1045	[25]
			5	846	
Los Angeles Latino Eye Study	USA	2000	Baseline	6357	[26]
			4	4658	

*Only one reference per study given.

88.1%) aged 50 years and above underwent ophthalmic and/or general examinations.

The prevalence of blindness and visual impairment [6], glaucoma, age-related macular degeneration (AMD) [27], diabetic retinopathy (DR), cataract, refractive error (RE) [28,29] and cardiovascular diseases [30,31] were assessed. This 2007/08 survey forms the baseline to cohort described here.

The overall aim of this cohort is to estimate the incidence, progression and risk factors for the development of blindness/visual impairment and their leading causes in a Kenyan adult population.

Objectives

Incidence

To estimate the age- and sex- specific incidence of visual impairment (VA < 6/12) and blindness (VA < 3/60) (all causes) in a Kenyan adult population.

To estimate the age- and sex- specific incidence of cataract, RE, glaucoma, AMD and DR.

Causes & risk factors

To identify the causes and risk factors for incident visual impairment and blindness from specific diseases investigated (specifically focusing on demographic, anthropometric, behavioural, and vascular risk factors).

Progression

To estimate the risk of progression of Cataract, RE, Glaucoma, AMD and DR among cases detected at baseline.

Treatment & progression outcome

To describe the outcome of treatment for cataract, RE, glaucoma or DR among cases detected at baseline.

To describe the progression of untreated eye disease among cases detected at baseline.

Methods/Design

This paper describes the definitions, eligibility criteria, follow-up procedures, visual acuity (VA) measurements, anthropometry and clinical examination procedures adopted for the study.

Baseline study population - sample size

The sample size of 5000 participants required for the baseline survey was calculated based on an expected prevalence of VA < 6/12 in the better eye due to posterior segment eye diseases (PSED) of 3.0% among those aged ≥50 years, a required precision of 0.5% (i.e. a 95% confidence interval [CI] of 2.5%-3.5%), a design effect of 1.5, and a response rate of 90%. (Epi Info 6.04, Centers for Disease Control and Prevention, Atlanta, GA). We selected 100 clusters each of 50 participants.

Sampling strategy and recruitment

Recent census data for Kenya were not available [32], and therefore electoral role lists that were renewed in 2006 in preparation for the 2007 general elections were used as the sampling frame for this baseline survey. The population size was updated for the year 2007 using a population growth rate of 2.7% per year [33]. One hundred clusters were selected with a probability proportional to the size of the population (Figure 1). A cluster was defined as the area served by the polling station.

Households were selected within clusters using a modified compact segment sampling method [34]. Each cluster was divided into segments so that each segment included approximately 50 people aged ≥ 50 years. For instance, if a cluster included 200 people aged ≥ 50 years then it was divided into four segments. One of the segments was chosen at random by drawing lots and all households in the segment were sequentially sampled, until 50 people aged ≥ 50 years were identified. An eligible individual was defined as someone aged ≥ 50 years living in the household for at least three months in the previous year. Age was determined using the subject's testimony, national identity cards and a calendar of historic events. If the segment did not include 50 people aged ≥ 50 years then another segment was chosen at random and sampling continued until 50 were reached. If after enumerating individual number 49 the next household had more than one person aged ≥50 all were enumerated and invited for examination.

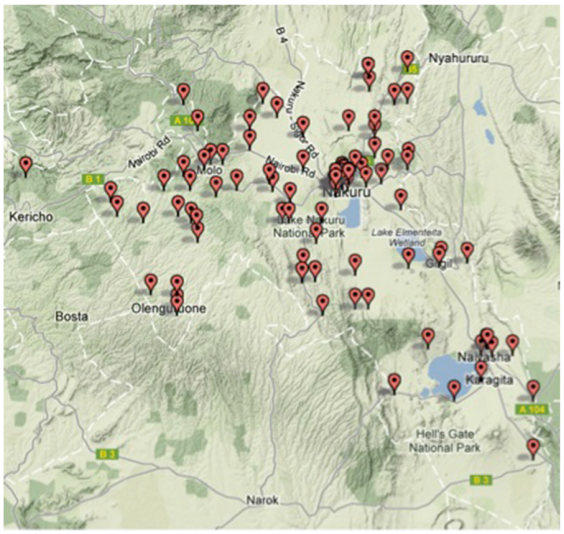

Figure 1 Map showing the 100 study locations in the Nakuru County, Kenya.

Baseline findings

In total, 4381 participants underwent complete (ophthalmic and general) examination at baseline across 100 clusters. The prevalence of blindness was 1.6% (95% CI: 1.2-2.1%) [6].

Follow-up

A pilot follow up retraced 438 participants from 10 of the 100 clusters in 2008, a mean of 1.5 years from baseline, and 408 (79%) were successfully retraced to give an estimated 4.2% loss per year.

Retracing at follow-up - advance team

Approximately one week before the follow-up examination clinic was planned for a given cluster, a field officer studied the maps of the village and made phone contact with the village chief or guide to arrange the visit. At the planning visit a list of study participants were given to the chief and a local village guide was recruited to assist location of the study participants. At this visit the examination site was established and identification of amenities such as electricity, water and road access were made. Two days prior to the clinic, the field officer reminded chiefs of the visit by phone and notified them and the guide of the advance team's arrival.

On the day prior to the examination clinic, the Advance Team visited homes of baseline participants and confirmed their identity using National Identity cards. The two advance teams comprised of one nurse, one field officer and a driver or public transport. During this visit they performed the following duties:

- Located individuals with assistance from the guide, phone numbers when available and previously recorded GPS locations using a Garmin Oregon 450 Satellite Navigation device.
- Explained details of the exam and obtain written/thumb print informed consent for examination
- Informed selected participants about location and time for examination

Registration

On the examination day, the advance team confirmed the identity of participants against their records from the previous day and against data from baseline (age, date of birth, name, and identity cards). Each participant was given a questionnaire, which was completed by the examiners as they move from station to station.

Examination procedures

Examinations were performed as per baseline unless otherwise indicated in Table 2.

Details of each examination station are provided below including differences, if there were any, between baseline and follow-up.

Anthropometry

A nurse performed and recorded measures of participants: height; weight; waist and hip circumference, and three measures of blood pressure, each 5 minutes apart. In addition, at follow-up, bioimpedence (Tanita Segmental Body Composition Monitor) was performed.

At baseline, capillary blood was taken from all participants for random blood glucose and cholesterol. At follow-up, no blood for cholesterol was collected and in addition, subjects with a random blood sugar greater than 11.1 mmol/L (IDF guidance at time of baseline study), those with known diabetes (regardless of random measure), evidence of diabetic retinopathy on retinal imaging and a subset (chosen randomly within each cluster) with random glucose between 7-11 mmol/L had an additional capillary blood HbA1c (A1C Now+, Bayer).

Interview

An interviewer performed the structured interview in the participant's preferred language covering i) demographic details including; name, year of birth, ethnicity and education level; ii) past medical and ocular history including medical or ophthalmic medication or surgery and relevant family history; iii) relevant risk factors including; smoking and tobacco consumption and alcohol intake; iv) socioeconomic status based on job, housing conditions, ownership of material goods and livestock which is translated in to a score based on previous work in the same population [35]. (See Additional file 1: Appendix for Questionnaire/Data Entry Booklet).

Visual acuity

A clinical officer determined whether the study participant:

a) Attends wearing distance correction glasses
b) Owns distance correction glasses but failed to bring them
c) Does not have any distance glasses
d) Routinely uses reading glasses
e) Attends wearing aphakic glasses

Visual acuity (VA) was measured using a back-illuminated modified LogMAR reduced tumbling E chart [36,37], which has been used in previous population based studies [38,39].

Autorefraction

All subjects, regardless of VA underwent autorefraction using the Topcon® Auto refractor RM8800 at baseline and the hand held SureSight autorefractor (Welch Allyn) at follow-up, following manufacturers guidelines. Any subject recording an acuity of ≤24 optotypes, <6/9 equivalent (with or without glasses) underwent best corrected visual acuity. The refraction measure recorded for each eye was mounted in the trial frames using trial lenses (rounded up or down to the nearest 0.25 diopters). Visual acuity was then re-measured to give an estimate of the "corrected visual acuity" in each eye individually. When autorefraction results were not available, the pinhole method was used to estimate corrected visual acuity. A subset of participants also underwent manual refraction by a visiting optometrist for five clusters to validate the accuracy of the autorefractor.

Visual field assessment

At baseline, all individuals with suspect or abnormal discs on clinical examination underwent automated visual field testing. The Humphrey® Field Analyzer II - 720*i* series (Carl Zeiss Ophthalmic Systems, Inc.) was used. A suspect or abnormal disc was defined as a vertical cup/disc ratio (VCDR) of 0.7 or above; optic disc cupping asymmetry between the eyes of more than 0.2 VCDR; or any other abnormal features. A random sample of five individuals per cluster (10%) also underwent visual field testing to provide normative data.

Participants performed the Swedish Interactive Thresholding Algorithm (SITA) STANDARD 24–2. SITA Fast was used to determine the threshold level in all participants having visual field analysis. Appropriate corrective lenses for refractive errors were used when needed. An automated fixation monitor was used throughout. If the SITA fast test was reliable (following manufacturers guidelines) the SITA standard test was performed. If the SITA fast was unreliable then this was repeated once. If it remained unreliable then no further testing was done.

At follow-up, a different strategy for visual field testing was used: All subjects with VA equivalent to > =6/60 Snellen underwent automated visual field testing by a trained visual field technician using the Henson 8000 Visual Field Analyser (TopCon, Inc.) The multiple stimulus suprathreshold test was used following manufacturers

Table 2 Instruments used at baseline and follow-up for examination, including rationale for change where appropriate

Procedure	Baseline Instrument (2007/08)	Follow-up instrument (2013/14)	Rationale for change
Near Vision Test	Continuous Text "Read in Style®" diopter chart	Unchanged	N/A
Personal Interview	Questionnaire developed by the survey ophthalmologist (WM)	Questionnaire developed by the survey ophthalmologist (AB) see Additional file 1: Appendix	N/A
Weight	The Seca 761 Medical Class 4 Scales mechanical ground scale (Williams Medical Supplies, London)	Tanita Segmental Body Composition Monitor	Combined weight and bioimpedence device – approved for medical studies
Bioimpedence	Not performed	Tanita Segmental Body Composition Monitor	Combined weight and bioimpedence device – approved for medical studies
Height	Leicester Height Measure (Stadiometer) (Chasmors Ltd, London)	SECA Height Measure	Better stability on uneven grounds
Waist and Hip circumference	Chasmors WM02 Body Tape measure	SECA Measuring tape	Availability
Blood pressure	Omron® Digital Automatic Blood Pressure Monitor Model HEM907	Unchanged	N/A
Visual Acuity	ETDRS LogMAR chart	Unchanged	N/A
Auto refraction	Topcon® Auto refractor RM8800	Welch Allyn SureSight	Improved portability
Corrected Visual Acuity	Frames and standard refraction lenses	Unchanged	N/A
Undilated eye exam including imaging (SL-OCT)	Haag-Streit® Slit lamp BD900 with SL-OCT	Haag-Streit® Slit lamp BM900 – no SL-OCT	Availability
Tonometry	Haag Streit® Goldmann Applanation tonometer on above slit lamp	Haag Streit® Goldmann Applanation tonometer on above slit lamp	N/A
Gonioscopy	Not performed	Four-mirror non-coupling gonioscopy lens (Zabby's)	For glaucoma sub-typing and angle evaluation in normal population
Visual fields	Humphrey Field Analyzer II -720 *i* series(Zeiss®)	Henson 8000 Visual Field Analyser (TopCon, Inc)	Deemed more suitable for epidemiological data collection
Pupil Dilation	Mydriacyl drops (Alcon®)	G. Tropicamide 1% + G. Phenylepherine 2.5% (Minims)	Single units and better shelf life
Blood sugar	Accutrend GCT and test strips (Roche®)	OneTouch Select, Lifescan	Availability. Approved for medical studies
Blood Cholesterol	Accutrend GCT and test strips (Roche®)	Not performed	Cost prohibited inclusion
HbA1c	Not performed	(A1C Now+, Bayer)	Increase accuracy of Diabetes Mellitus diagnosis as participants non-fasted
Examination of anterior and posterior segments through a dilated pupil	90D lens and slit lamp(Volk®)	Superfield and 60D Lens (Volk) and Slit Lamp	Study ophthalmologist preference
Retinal Photo	Topcon® NW6S Non Mydriatic camera model	Haag-Streit DRS Retinal Camera	Suitability for travel and ease of use.

guidelines (Screening test - 26 test locations). When one or more spots were missed, the 26-point test was repeated for that eye. If any missed spots re-occurred on the second time of testing the test for that eye was extended to 68 test locations. This machine and strategy were used in preference to the baseline methods due to feedback from both patient's and tester at baseline. Patient's found the baseline testing protocol difficult to understand and the time required to complete the test meant only a sub-sample of the population could be investigated.

Slit lamp biomicroscopy examination

Undilated (anterior segment) and dilated (posterior segment) slit lamp biomicroscopy examination were performed on all participants by the study ophthalmologists (WM at baseline, AB at follow-up) using a

Haag-Streit BD 900 Slit Lamp (BM 900 at follow-up) and Volk condensing lenses (90D at baseline, Superfield and 66D at follow-up).

Anterior segment

The anterior segment of the eye was assessed for the presence of signs of trachoma. In addition at follow up examination included grading of corneal scarring, pterygium, secondary glaucoma, evidence of past or active uveitis, or evidence of surgery. The angle at baseline and follow-up was assessed using the Van Herick Test [40] and direct visualization of the angle using gonioscopy (performed after intraocular pressure, see below) was performed at follow-up.

At follow-up, the ophthalmologist using a bright LED pen torch tested for the Relative Afferent Pupil Defect (RAPD). RAPD was recorded as present or absent. If present it was sub-categorised in to "subtle" or "definite".

Intraocular pressure

Goldmann Applanation Tonometry (GAT) was used to measure intraocular pressure (IOP). A drop of Proxymethacaine and fluorescein (minims) were instilled to each eye. After 20 seconds the GAT was used in combination with a slit lamp to measure the IOP in each eye. The GAT's calibration was checked as per manufacturers instructions on a daily basis by the study ophthalmologist, if found to be inaccurate, the spare GAT was used whilst the original was returned to the factory for calibration. One reading was taken from each eye and the GAT was disinfected between patients.

Gonioscopy

Assessment of the opening angle of participants' right and left eyes was made using a four-mirror gonioscopy lens (Zabbys). This lens does not require coupling fluid and was chosen to minimize impact on the quality of retinal photographs. Angles were recorded using standard Shaffer grading [41] and further classified as "open", "occludable" or "closed" based on standard referral criteria. Occludable angles are defined as: pigmented trabecular meshwork not visible in 3⁄4 or more of angle circumference in primary position without manipulation, in presence of low illumination. If the patient could not cooperate with gonioscopy, the Van Herick (VH) technique [40] was used for grading.

Dilated slit lamp examination

Pharmacologic dilation of the subject's pupils was achieved by using tropicamide 1% (Mydriacyl) with phenylephrine hydrochloride 2.5% if needed. Dilation was not performed in subjects deemed at risk of narrow angle closure (inability to visualise at least 180° of posterior pigmented trabecular meshwork on non-indentation gonioscopy [42]). At risk subjects were referred to the Nakuru Eye Unit for prophylactic laser peripheral iridotomies.

Lens

The WHO simplified system for lens grading was used [43] following standard protocols. The lens was also examined for position, the presence of hyper mature (Morgagnian) cataract, and previous lens surgery (aphakic or pseudophakic). A red reflex lens image was taken when each participant was having retinal photographs. At follow-up, pseudophakic participants were assessed for the presence or absence of posterior capsular opacification and, if present, whether it entered the visual axis.

Optic disc

The optic nerve head was examined using a 90 Diopter Lens (Volk) at the slit lamp at baseline and a 66 Diopter lens (Volk) at follow-up. The clarity of the optic nerve head was determined and graded as clear, hazy or no view. Among subjects in whom an adequate view of the disc was obtained, the VCDR was estimated and recorded for each eye. Other glaucomatous changes were recorded and non-glaucomatous characteristics such as optic atrophy and optic pits were also recorded.

Macula

The macula was examined using a 90 Diopter Lens (Volk) at the slit lamp at baseline and a 66 Diopter or Superfield lens (Volk) at follow-up. The view of the macula was recorded as clear, hazy or no view. DR was clinically graded and recorded as absent, non proliferative, proliferative and end stage or maculopathy (macula oedema) [44]. The presence of drusen, hypo or hyper pigmentation, dry or geographic atrophy and neovascular changes were also recorded.

Fundus photography

An Ophthalmic Assistant performed digital photography of the lens and fundus on all study participants using a Topcon® NW6S Non Mydriatic camera model at baseline and DRS Digital Fundus Camera (Haag-Streit) at follow-up. The study ophthalmologist checked images were of sufficient quality for grading in the absence of prominent media opacities. An anterior segment co-axial photograph was taken for lens grading from each eye. Two 45° fundus photographs were taken in each eye, one optic disc centered and the other macula centered. Images were then securely uploaded to the Moorfields Reading Centre for review and grading for image quality, the presence or absence of pathology and the severity of pathology when present.

Note: The gold-standard for grading of DR, AMD and optic disc changes is based on retinal photographs and not clinical assessment. Clinical examination was performed as a backup to equipment failure and a comparison of clinical

and image based grading can be compared in the analysis stage and factored in the scenario by which a number of participants only have clinical grading available.

Data management and analysis

A patient record was completed for each participant and crosschecked for errors by the project field coordinator. Patient records were scanned to create a digital backup and then data were entered into an EpiData database (with built in range and consistency checks) independently by two data clerks and validated by the study ophthalmologist to reconcile any differences. Further data cleaning and all statistical analyses were conducted using STATA 10.0 (StataCorp LP, Texas, USA).

The visual fields PDF print outs and raw data were sent securely to Moorfields Eye Hospital for grading along with the fundus and anterior segment images at baseline and follow-up. All image and visual field data were backed up on local devices and external hard drives. All images were first examined for quality and categorized as excellent, good, fair, borderline and ungradeable. If the images were ungradeable the clinical diagnosis was used. For gradable images the retina and optic disc were reviewed, and a diagnosis made based on the appearance of the image e.g. diabetic retinopathy, toxoplasmosis, onchocerciasis, age related macular degeneration, myopic fundus, glaucoma, optic atrophy or other retinal pathology. VCDR was measured and all images were graded for the absence/presence and stage of DR and ARMD. The graders graded the images for as many disease categories as possible, and so if it was feasible to grade an image for optic disc abnormality but not for ARMD, then the grader completed the optic disc grading only. A senior grader verified a random 10% of images that were graded as normal as well as all abnormal images to ensure quality assurance. The graders re-graded a random selection of images with a minimum of 14-days interval to allow for intragrader reliability to be established.

Definitions used for analysis are detailed in Table 3.

Quality assurance procedures

Training

Inter observer variations (IOV) assessments were performed in the training phase. IOV assessments on anthropometric variables were done by having the two nurses perform repeat measuring of 50 subjects. IOV of visual acuity were undertaken by having the ophthalmic clinical officer (OCO) and ophthalmic nurse repeat measures of 50 subjects (half normal vision and half visual impairment). IOV of undilated examinations were done by repeat measure of 50 subjects (half normal vision and half visual impairment) by a visiting ophthalmologist and study

Table 3 Definitions of disease incidence and progression

Disease	Incidence		Progression	
Definition	**At risk**	**Cases**	**At risk**	**Cases**
Blindness and Visual Impairment (VI)	Blind: Persons with VA of ≥3/60 in the better eye at baseline.	Persons who have VA of <3/60 in the better eye at follow up who had ≥3/60 in the better eye at baseline	Categorical changes in visual acuity between: Normal; Mild VI; Moderate VI; Severe VI; Blind, with a minimum of two line Snellen equivalent change in VA.	
Cataract	Persons without evidence of cataract at baseline based on WHO simplified cataract grading systems	Persons with evidence of cataract at follow-up based on WHO simplified cataract grading systems [45] who did not have evidence at baseline	Persons with evidence of any grade of cataract at baseline based on WHO simplified cataract grading systems	Persons who increase by two or more severity grades in each sub-type of cataract.
Primary open angle glaucoma	Persons without glaucoma in either eye at baseline based on ISGEO [46] criteria	Persons who develop ISGEO classification 1, 2 or 3 glaucoma by the 6-year follow-up point	Glaucoma or glaucoma suspect case at baseline	Definite, disc or field progression. See below* [47]
Age-related macula degeneration	Persons who did not have any evidence of AMD at baseline in both eyes	Persons with evidence of early, late or specific AMD lesions	AREDS [48] step 9 or less (no AMD or early AMD) at baseline.	2-or-more-step increase in combined AREDS score from baseline in persons with gradable fundus photographs at both time points.
Diabetic retinopathy	Persons with diabetes and free of retinopathy at baseline and persons developing DM by follow up.	Persons with signs of DR (ETDRS) [49] CSME and incidence of proliferative or severe DR$^{\Upsilon}$	Persons with diabetes and minimal or moderate DR at baseline	(1) Persons who develop severe DR by the 6-year follow-up (2) Increase by ≥ 3 steps on the ETDRS Severity Scale or development of proliferative DR necessitating photocoagulation therapy or vitrectomy

**Definite progression* will be defined as those with a combination of ≥0.2 VCDR increase in either eye and/or ≥0.2 VCDR asymmetry between the two eyes with a corresponding progression on the visual field test defined as (TBC – either "expert analysis" or an arbitrary objective measure).
Note: More specific definitions will be provided in subsequent papers.

ophthalmologist at the beginning of the baseline survey and again in the middle. IOV of dilated exams were done by repeat measure of 50 subjects (half normal vision and half visual impairment) by a visiting ophthalmologist and study ophthalmologist at baseline. Retraining was done where IOV scores indicated poor comparability (kappa < 0.5).

At follow-up, four weeks of training in November/December 2012 was completed for the study team members on all equipment and study protocols. Three pilot clusters examining over one hundred people were completed prior to commencing the study.

Standard Operating Procedures (SOP) detailing follow-up survey methodology for each examination station were prepared and read by all study team members. The SOP was used in training and for reference during fieldwork. Supervisory visits were made to the field site (HK and MJB) to monitor practices and ensure standard protocols were being followed.

Non-responders at follow-up

Participants who were examined at baseline and eligible for follow-up assessment but who did not attend the examination clinic were contacted to determine the reason for their absence. Participants who were not locatable for the examination were categorized as non-responders and their reason for absence determined through available phone contact, neighbors and village guides as, "deceased", "moved away", or "unknown".

Service provision

All participants identified with treatable disease in the study were offered appropriate care including free surgery and transport to the Rift Valley General Provinical Hospital or St Mary's mission hospital, Elementita. Specific cases requiring other services were referred to the Kikuyu Eye Unit. A trained ophthalmic nurse or Ophthalmic Clinical Officer (OCO) discussed the diagnosis and the treatment options available to subjects diagnosed with untreatable eye disease. As well as study participants, non-study attendees were examined and treated by the study team.

Ethical approval

The study adhered to the tenets of the Declaration of Helsinki and was approved by the Ethics Committee of London School of Hygiene and Tropical Medicine at both baseline and follow-up. Baseline approval was provided by the Kenya Medical Research Institute and the African Medical and Research Foundation (AMREF), Kenya at follow-up. At both phases approval was also granted by the Rift Valley Provincial Medical Officer and the Nakuru district Medical Officer of Health. Approval was sought from the administrative heads in each cluster, usually the village chief. They were also given a copy of the consent form to read and pass on to those in the village.

Informed consent

Informed consent was obtained from all participants. The objectives of the survey and the examination process were explained to those eligible in the local dialect, in the presence of a witness. A subject was examined only after informed consent was obtained. All participants gave written (or thumbprint) consent to participate.

Discussion

The Nakuru Eye Disease Cohort Study is the first population-based cohort study of eye disease to have taken place in Africa. It will provide estimates on the incidence of blindness and visual impairment, the incidence and progression of: cataract, refractive error, glaucoma, ARMD and DR as well other retinal conditions. This data will be disseminated to eye care providers and programs in the region to facilitate the provision of eye care services.

Additional file

Additional file 1: Appendix. The Nakuru Eye Disease Cohort Study - Study Questionnaire 2013.

Abbreviations

AMD: Age related macular degeneration; AREDS: Age Related Eye Disease Study; CI: Confidence interval; CSME: Clinically significant macula oedema; D: Dioptres; DR: Diabetic retinopathy; ETDRS: Early Treatment of Diabetic Retinopathy Study; GAT: Goldmann Applanation Tonometry; GPS: Global Positioning System; HbA1c: Haemoglobin 1c; ISGEO: International Society for Geographical Epidemiological Ophthalmology; LogMAR: Logarithm of the minimal angle of resolution; OCO: Ophthalmic clinical officer; PSED: Posterior segment eye diseases; RAAB: Rapid assessment of avoidable blindness; RAPD: Relative Afferent Pupil Defect; RE: Refractive error; SOP: Standard Operating Procedures; VA: Visual acuity; VCDR: Vertical cup to disc ratio; VH: Van-Herrick; VI: Visual impairment; WHO: World Health Organization.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

Conceptualization and formulation of study protocol; AB, WM, HK, MJB, TP, AF. Training; AB, WM, HR. Monitoring of Study Implementation; AB, HR, MJB, HK. Reading and revising manuscript: MJB, TP, HK, AB, HW, HR, WM, AF. Data cleaning; AB, HW. Data Analysis; AB, HW, HK, MJB. All authors read and approved the final manuscript.

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Study ID ☐☐☐-☐☐

The Nakuru Eye Disease Cohort Study

-

Study Questionnaire 2013

REFERRALS		
DIABETIC	☐ Yes – **REFER**	**READING GLASSES DISPENSED? POWER**
Distance GLASSES	☐ Yes - **REFER**	
CATARACT	☐ Yes - **REFER**	**Any other treatment? E.g. drops**
GLAUCOMA	☐ Yes - **REFER**	
DIABETIC RETINOPATHY	☐ Yes - **REFER**	
OTHER	☐ Yes - **REFER**	

Study ID ☐☐☐-☐☐

Mark Tick Boxes using a black biro with a cross "X", if marked incorrectly, fill in the box and mark the correct box.

e.g. ☒ if incorrect fill the box → ■

Answer Questions in the grey boxes

Phase	Section	Page	Complete?
1	**Registration/Demographic Data [A]**	3	☐
	Autorefraction [B]	4	☐

Phase	Visual Acuity [A]	Interview [B]	Height/Weight etc. [C]	Slit Lamp – Undilated [D]	Visual Fields [E]
2	☐	☐	☐	☐	☐
Page	5-7	8-12	13	14-16	17

All tests above this line must be completed before pupil dilation

Phase	Section	Page	Complete?
3	**Dilated Slit Lamp Examination**	18-22	☐
	Fundus Camera	23	☐

Study ID ☐☐☐-☐☐

1. A. Demographic data (Registration Desk)

Cluster Number	3 digit number 001-100					
Individual Number	2 digit number 01-50					
Study ID Number	Cluster Number – Individual Number				--		
Date of the examination	Day / Month / Year (dd/mm/yyyy)					
First name	text					
Last name	text					
Common name	text					
ID Number	from ID Card if available					
Serial Number	from ID Card if available					
Village name						
Telephone number						
Whose telephone is this?						
Sex	☐ Male (1)	☐ Female (2)				
Date of birth	Date / Month / Year If year only known enter 99/99/19YY	dd	mm	19	yy	
Age	in years (55+)					
Ask "mother tongue"	☐ Kikuyu (1)	☐ Kalenjin (2)				
	☐ Kisii (3)	☐ Luo (4)				
	☐ Luhyia (5)	☐ Masaai (6)				
	☐ Kamba (7)	☐ Other (8)				
Highest level of Education	☐ Primary (1)	☐ Secondary (2)	☐ College/University (3)	☐ None (4)		

I have recorded the data onto the form:

Name **Date**

Study ID ☐☐☐-☐☐

1. B. Refraction (Ophthalmic Nurse)

Refraction? (Select ONE only)	**Right Eye**	**Left Eye**
	☐ AutoRefraction possible	☐ AutoRefraction possible
	☐ AutoRefraction not possible	☐ AutoRefraction not possible
	☐ Manual Refraction	☐ Manual Refraction
Refraction Result	**Right Eye**	**Left Eye**
Sphere +/- 00.00 (to nearest 0.25)		
Cylinder +/- 00.00 (to nearest 0.25)		
Axis 0-180		
Reliability score (1 to 9)		

Print out Autorefraction and attach to back of booklet

Study ID ☐☐☐-☐☐

2.A. Presenting Vision (Ophthalmic Nurse)

Glasses (Select **ONE** only)	☐ Wearing distance glasses (Go to 2.A.a)
	☐ Has no distance glasses (Go to 2.A.b)
	☐ Forgot distance glasses (Go to 2.A.b)

Wears glasses for reading	☐ Yes	☐ No
Wears aphakic glasses (has had cataract surgery)	☐ Yes	☐ No

2.A.a

Test vision WITH glasses if available. If own glasses not available skip to Question 2.A.b (page 6).

Vision WITH distance or aphakic glasses at 4m	Number of letters seen at 4 meters (0 to 39)	**R**	**L**
If Visual Acuity Recorded at 4 meters (greater than 00) in either eye move to next station *If misses top E at 4m, move to 1m and retest (Record 00 at 4m)*			

Vision WITH distance or aphakic glasses at 1m	Number of letters seen at 1 meter (0 to 39)	**R**	**L**
If misses top E at 1m, move to next box (Record 00 at 1m)			

If cannot see at 1m *(Select ONE only)*	**Right Eye**	**Left Eye**
	☐ Counting fingers at 1m	☐ Counting fingers at 1m
	☐ Hand Movements	☐ Hand Movements
	☐ Perception of light	☐ Perception of light
	☐ No light perception (in dark)	☐ No light perception (in dark)

Study ID ☐☐☐-☐☐

2.A.b (not needed if vision was tested with own glasses)

Vision WITHOUT glasses at 4m	Number of letters seen at 4 meters (0 to 39)	**R**	**L**
If Visual Acuity Recorded at 4 meters (greater than 00) in either eye move to next station *If misses top E at 4m, move to 1m and retest (Record 00 at 4m)*			

Vision WITHOUT glasses at 1m (if 00 at 4m)	Number of letters seen at 1 meter (0 to 39)	**R**	**L**
If misses top E at 1m, move to next box (Record 00 at 1m)			

If cannot see at 1m *(Select ONE only)*	**Right Eye**	**Left Eye**
	☐ Counting fingers at 1m	☐ Counting fingers at 1m
	☐ Hand Movements	☐ Hand Movements
	☐ Perception of light	☐ Perception of light
	☐ No light perception (in dark)	☐ No light perception (in dark)

Study ID ☐☐☐-☐☐

2.A.c

Is Best Corrected Visual Acuity (Wearing refraction results) Indicated From Page 4 (Select **ONE** only)	**Vision in Best Eye**
	☐ Not indicated (could read 25 or more letters in the best eye) ***Move patient to next station*** *(miss page 7)*
	☐ Indicated (could not read 25 or more letters in the best eye, **refraction not available therefore use pinhole.**

NOW TEST BEST CORRECTED/PIN HOLE VISUAL ACUITY IF LESS THAN 25 LETTERS SEEN IN BETTER EYE

How was corrected vision tested (Select **ONE** only)	☐CORRECTED WITH LENSES
	☐CORRECTED WITH PINHOLE If refraction was not possible
	☐CORRECTED VISION NOT TESTED

Using refraction result from Section 1.B, page 4.

BEST CORRECTED VISUAL ACUITY at 4m	Number of letters seen at 4 meters (0 to 39)	**R**	**L**
Move to next station if Best Corrected Visual Acuity Recorded at 4 meters (greater than 00) *If misses top E at 4m, move to 1m and retest (Record 00 at 4m)*			

BEST CORRECTED VISUAL ACUITY at 1m	Number of letters seen at 1 meter (0 to 39)	**R**	**L**
If misses top E at 1m, Record 00 at 1m			

I have recorded the data onto the form:

Name **Date**

Study ID ☐☐☐-☐☐

2.B. General Heath (Nurse/Interviewer)

Have you ever been diagnosed with diabetes?	☐ Yes (1)	☐ No (2)			
					If NO, go to next question
How long ago were you diagnosed with diabetes?	Years (01 – 99) If less than one year, enter "01"				
Are you receiving treatment for diabetes? (select **ALL** that apply)	☐ Yes, insulin (1)	☐ Yes, tablets (2)	☐ Yes, diet (3)	☐ Yes, traditional (4)	☐ No (5)

Have you ever been diagnosed with high blood pressure?	☐ Yes (1)	☐ No (2)		
				If NO, go to next question
How long ago were you diagnosed with high blood pressure?	Years (if less than 1 year mark "0"			
Are you receiving treatment for high blood pressure? (select **ALL** that apply)	☐ Yes, tablets (1)	☐ Yes, diet (2)	☐ Yes, traditional (3)	☐ No (4)

Have you been diagnosed or are you suffering from any of the following? (tick all that apply)	☐ Renal Disease (1)	☐ Heart Disease (2)	☐ Foot Ulcers (3)	☐ None (4)
Did/Do your **mother** have any of the following?	☐ Diabetes (1)	☐ High Blood Pressure (2)	☐ Blinding eye condition (3)	☐ Not sure/None (4)
Did/Do your **father** have any of the following?	☐ Diabetes (1)	☐ High Blood Pressure (2)	☐ Blinding eye condition (3)	☐ Not sure/None (4)
Did/Do your **siblings** have any of the following?	☐ Diabetes (1)	☐ High Blood Pressure (2)	☐ Blinding eye condition (3)	☐ Not sure/None (4)

Study ID ☐☐☐-☐☐

2.B. continued: Blood Pressure (Nurse)

Take First and Second Blood Pressure Measurements			
First Blood Pressure Reading	Systolic (00 to 250)	Diastolic (00 to 250)	Pulse (00 to 250)
Wait ten minutes between readings. Ensure patient is resting, sitting and no talking whilst BP being taken			
Second Blood Pressure Reading	Systolic (00 to 250)	Diastolic (00 to 250)	Pulse (00 to 250)

Do you drink alcohol? (Answer **ONE** only)	☐ Daily/Most days (1)	☐ Weekends only (2)	☐ 1-2 times per month (3)	☐ Special occasions only (4)	☐ Never (5)	☐ Former (>6 months) (6)

Have you ever smoked?	☐ Never (1)	☐ Former (stopped > 6 months ago) (2)		☐ Current (in last 6 months) (3)	
If "Never", skip to next question					
		Age at starting	years		
		Duration of use	years		
		Number of days per week	days (max 07)		
		Number smoked per day			

Have you ever snuffed tobacco?	☐ Never (1)	☐ Former (stopped > 6 months ago) (2)		☐ Current (in last 6 months) (3)	
If "Never", skip to next question					
		Age at starting	years		
		Duration of use	years		
		How many days used per week	days (max 07)		
		How many times used per day			

Study ID ☐☐☐-☐☐

2.B. continued

Have you ever chewed tobacco?	☐ Never (1)	☐ Former (stopped > 6 months ago) (2)		☐ Current (in last 6 months) (3)	
If "Never", skip to next page					
		Age at starting	years		
		Duration of use	years		
		Number of days per week	days (max 07)		
		Number chewed per day			

Study ID ☐☐☐-☐☐

2.B. Socioeconomic Status (Nurse/Interviewer)

In the last month have you had a job other than working in the field owned or rented by the household?	☐ Yes (1)		☐ No (2)
Major external wall material of your home (Select **ONE** only)	☐ Brick (1)	☐ Concrete Block (2)	☐ Stone (3)
	☐ Unbaked brick (4)	☐ Wood/logs (5)	☐ Tin, zinc sheeting (6)
	☐ Flattened tin cans (7)	☐ Mud (8)	☐ Stone and Mud (9)
	☐ Canvas/Felt (10)	☐ Other (11)	
Primary Roof Material of your home (Select **ONE** only)	☐ Concrete (1)	☐ Shingles (2)	☐ Asbestos Sheets (3)
	☐ Metal Sheets (4)	☐ Tile (5)	☐ Wood (6)
	☐ Unbaked bricks (7)	☐ Thatch (8)	☐ Other (9)
Primary Floor Material of your home (Select **ONE** only)	☐ Parquet (1)	☐ Painted wood (2)	☐ Tile (3)
	☐ Linoleum (4)	☐ Concrete (5)	☐ Clay/earthen floor (6)
	☐ Other (7)		
Where is the toilet? (Select **ONE** only) If more than one toilet mark best one	☐ Inside dwelling (1)		☐ Outside dwelling – in compound (2)
	☐ Outside dwelling – outside compound (3)		☐ Not Applicable/no access to a toilet (uses bush etc) (8)
Type of toilet? (Select **ONE** only) If more than one toilet mark best one	☐ Flush Toilet (1)	☐ Traditional latrine (2)	☐ Improved pit latrine with ventilation (VIP)(3)
	☐ Bowl/Bucket (4)	☐ Other (5)	☐ No toilet (6)

Study ID ☐☐☐-☐☐

Household assets (Select **ALL** that apply)	☐ Radio/Hifi	☐ Sewing machine
	☐ TV/VCR/DVD	☐ Table
	☐ Fridge/Freezer	☐ Bicycle
	☐ Telephone/cell phone	☐ Washing machine
	☐ Cupboard	☐ Motor vehicle/car
	☐ Sofaset/armchair	☐ Motorbike
How many of the following animals do you possess? *Enter "0" if none*	Cows?	
	Sheep?	
	Pigs?	
	Chicken/ducks?	

Blood Pressure

	Systolic (00 to 250)	Diastolic (00 to 250)	Pulse (00 to 250)
Third Blood Pressure Reading			

Treatment history and barriers to uptake (Nurse/Interviewer)

Previous Eye Surgery (Select **ALL** that apply)	**Right Eye**	**Left Eye**
	☐ Cataract Surgery	☐ Cataract Surgery
	☐ Eye lid surgery (Trachoma)	☐ Eye lid surgery (Trachoma)
	☐ Glaucoma Surgery	☐ Glaucoma Surgery
	☐ Other	☐ Other
	☐ No Surgery	☐ No Surgery
Current regular medicine for the eyes (Select **ALL** that apply)	**Right or Left Eyes**	
	☐ Antibiotics	
	☐ Steroids	
	☐ Anti-Glaucoma	
	☐ Lubricant	
	☐ Other	
	☐ No medicines	

Study ID ☐☐☐-☐☐

2.C. Anthropometry (Nurse)

Patient Age from page 3:	

Height in cm (no dp)		888: unable, 999: refused	
Weight in kg (1 dp)		888: unable, 999: refused	
Body Fat %		888: unable, 999: refused	
Muscle Mass		888: unable, 999: refused	
Bone MASS		888: unable, 999: refused	
Metabolic Age		888: unable, 999: refused	
Total Body Water %		888: unable, 999: refused	
Visceral Fat Level		01-59 888: unable, 999: refused	
Waist circumference **in cm** (no dp)		888: unable, 999: refused	
Hip circumference **in cm** (no dp)		888: unable, 999: refused	

Random blood sugar mmol/L	0.0 to 35.0	

If ≥ 11.1 mmol/l	HbA1c (%)	Enter number on screen (<4 or >13 may be shown)	

I have recorded the data onto the form:

Name **Date**

Study ID ☐☐☐-☐☐

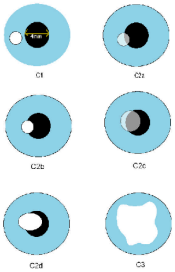
2.D. Anterior Segment Examination (Ophthalmologist)

Relative Afferent Pupil Defect	**Right Eye**		**Left Eye**	
	☐ Definite	☐ Subtle	☐ Definite	☐ Subtle
	☐ No	☐ Not able	☐ No	☐ Not able

Pterygium present and extent	**Right Eye**	**Left Eye**
	☐ No Pterygium	☐ No Pterygium
	☐ Pterygium – Cornea NOT involved	☐ Pterygium – Cornea NOT involved
	☐ Pterygium – Cornea Involved	☐ Pterygium – Cornea Involved
mm in to cornea from limbus (0-12)	☐☐	☐☐

Study ID ☐☐☐-☐☐

2.D. continued

Corneal scarring grade	Right Eye	Left Eye
	☐ NO Opacity	☐ NO Opacity
	☐ Opacity not entering central 4mm (C1)	☐ Opacity not entering central 4mm (C1)
	☐ Opacity within central 4mm but not entering within the central 1mm of the cornea. The pupil margin is visible through the opacity (C2a)	☐ Opacity within central 4mm but not entering within the central 1mm of the cornea. The pupil margin is visible through the opacity (C2a)
	☐ Opacity within central 4mm but not entering within the central 1mm of the cornea. The pupil margin is not visible through the opacity (C2b)	☐ Opacity within central 4mm but not entering within the central 1mm of the cornea. The pupil margin is not visible through the opacity (C2b)
	☐ Opacity within central 4mm and entering the central 1mm of the cornea. The pupil margin is visible through the opacity (C2c)	☐ Opacity within central 4mm and entering the central 1mm of the cornea. The pupil margin is visible through the opacity (C2c)
	☐ Opacity within central 4mm and entering within the central 1mm of the cornea. The pupil margin is not visible through the opacity (C2d)	☐ Opacity within central 4mm and entering within the central 1mm of the cornea. The pupil margin is not visible through the opacity (C2d)
	☐ Opacity large enough and dense enough to make whole pupil margin invisible (C3)	☐ Opacity large enough and dense enough to make whole pupil margin invisible (C3)
	☐ Phthisis (C4)	☐ Phthisis (C4)

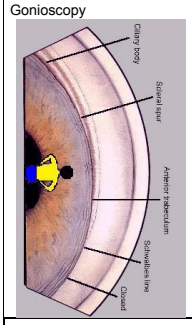
Anterior Segment	Right Eye	Left Eye
Mark **ALL** that apply	☐ Pseudoexfoliation	☐ Pseudoexfoliation
	☐ Iris Trans illumination	☐ Iris Trans illumination
	☐ Krukenberg's Spindle	☐ Krukenberg's Spindle
	☐ Evidence of previous inflammation	☐ Evidence of previous inflammation
	☐ None of the above	☐ None of the above

Study ID ☐☐☐-☐☐

2.D. continued

Van Herick's	Right Eye	Left Eye
	☐ ACD = 0 or negligible (0)	☐ ACD = 0 or negligible (0)
	☐ ACD ≤1/4 cornea (1)	☐ ACD ≤1/4 cornea (1)
	☐ ACD = 1/4 cornea (2)	☐ ACD = 1/4 cornea (2)
	☐ ACD =1/4-1/2 cornea (3)	☐ ACD =1/4-1/2 cornea (3)
	☐ ACD >=1/2 cornea (4)	☐ ACD >=1/2 cornea (4)
	☐ not gradable (9)	☐ not gradable (9)

Applanation IOP (mmHg)	99 = not possible	R	L

Gonioscopy	Right Eye	Left Eye
	☐ Nil (0)	☐ Nil (0)
	☐ Scwalbe's line and anterior meshwork (1)	☐ Scwalbe's line and anterior meshwork (1)
	☐ Posterior pigmented meshwork (2)	☐ Posterior pigmented meshwork (2)
	☐ Scleral Spur (3)	☐ Scleral Spur (3)
	☐ Ciliary Band (4)	☐ Ciliary Band (4)
	☐ Not gradable (5)	☐ Not gradable (5)

Safe to dilate? ☐ Yes ☐ No

Study ID ☐☐☐-☐☐

2.E. Visual Fields (Visual Field Technician)

VF completed?	**Right Eye**	**Left Eye**
	☐ Yes	☐ Yes
	☐ No – uncooperative	☐ No – uncooperative
	☐ No – poor visual acuity	☐ No – poor visual acuity
	☐ No – machine failure	☐ No – machine failure
Classification (in the field – by ophthalmologist or OCO)	**Right Eye**	**Left Eye**
	☐ Normal	☐ Normal
	☐ Abnormal – definite Glaucoma	☐ Abnormal – definite Glaucoma
	☐ Abnormal – suspect glaucoma	☐ Abnormal – suspect glaucoma
	☐ Abnormal – non-glaucoma	☐ Abnormal – non-glaucoma

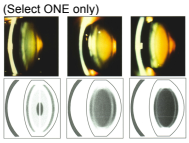
Print out Visual Fields and attach to back of booklet

I have recorded the data onto the form and printed the visual fields:

Name **Date**

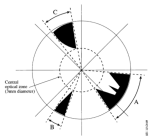
Study ID ☐☐☐-☐☐

3.A. Dilated Examination (Ophthalmologist)

WHO CATARACT GRADING (See Document for Reference)		
Cataract (Select ONE only) 3.A.1	**Right Eye**	**Left Eye**
	[0] ☐ No cataract	[0] ☐ No cataract
	[1] ☐ Gradable cataract	[1] ☐ Gradable cataract
	[2] ☐ Mature	[2] ☐ Mature
	[3] ☐ Hypermature	[3] ☐ Hypermature
	[4] ☐ Corneal Opacity	[4] ☐ Corneal Opacity
	[5] ☐ Phythsis	[5] ☐ Phythsis
	[7] ☐ Aphakia	[7] ☐ Aphakia
	[8] ☐ IOL	[8] ☐ IOL
	[9] ☐ Can not grade	[9] ☐ Can not grade
Nuclear (Select ONE only)  1 2 3	**Right Eye**	**Left Eye**
	☐ Not applicable	☐ Not applicable
	☐ Nuclear 0 [0]	☐ Nuclear 0 [0]
	☐ Nuclear 1 [1]	☐ Nuclear 1 [1]
	☐ Nuclear 2 [2]	☐ Nuclear 2 [2]
	☐ Nuclear 3 [3]	☐ Nuclear 3 [3]
	☐ Aphakia [7]	☐ Aphakia [7]
	☐ IOL [8]	☐ IOL [8]
	☐ Cannot grade [9]	☐ Cannot grade [9]

Study ID ☐☐☐-☐☐

3.A. continued

Cortical (Select ONE only)  0: <1/8, 1: 1/8 to <1/4, 2: ¼ to <1/2, 3: 1/2+	**Right Eye**			**Left Eye**		
	☐ Not applicable			☐ Not applicable		
	☐ Cortical 0 [0]			☐ Cortical 0		
	☐ Cortical 1 [1]			☐ Cortical 1		
	☐ Cortical 2 [2]			☐ Cortical 2		
	☐ Cortical 3 [3]			☐ Cortical 3		
	☐ Aphakia [7]			☐ Aphakia		
	☐ IOL [8]			☐ IOL		
	☐ Cannot grade [9]			☐ Cannot grade		
Cortical Central? (central 3mm)	☐ Yes [1]	☐ No [2]	☐ N/A [3]	☐ Yes [1]	☐ No [2]	☐ N/A [3]

Posterior Subcapsular (PSC) (Select ONE only) 0: <1mm 1: >=1mm, <2mm 2: >=2mm, <3mm 3: >=3mm	**Right Eye**	**Left Eye**
	☐ Not applicable	☐ Not applicable
	☐ PSC 0 [0]	☐ PSC 0 [0]
	☐ PSC 1 [1]	☐ PSC 1 [1]
	☐ PSC 2 [2]	☐ PSC 2 [2]
	☐ PSC 3 [3]	☐ PSC 3 [3]
	☐ Aphakia [7]	☐ Aphakia [7]
	☐ IOL [8]	☐ IOL [8]
	☐ Cannot grade [9]	☐ Cannot grade [9]
Posterior Capsular Opacification (PCO) with IOL	**Right Eye**	**Left Eye**
	☐ Yes - within central 3mm [1]	☐ Yes - within central 3mm [1]
	☐ No – Clear capsule [2]	☐ No – Clear capsule [2]
	☐ Not sure [3]	☐ Not sure [3]
	☐ Evidence of capsulotomy [4]	☐ Evidence of capsulotomy [4]
	☐ Yes – outside central 3mm [5]	☐ Yes – outside central 3mm [5]
	☐ N/A [9]	☐ N/A [9]

Study ID ☐☐☐-☐☐

3.A. continued

POSTERIOR SEGMENT EXAMINATION (1 in 10 participants and those in whom imaging not possible)		
☐ 1 in 10	☐ Imaging not possible	☐ Not applicable *(skip to 3B)*

View of PSED at slit lamp	**Right Eye**	**Left Eye**
	☐ Clear	☐ Clear
	☐ Hazy	☐ Hazy
	☐ No view	☐ No view

Vertical Cup to Disc Ratio	0.0 to 1.0	**R**	☐Can not assess	**L**	☐Can not assess
VCDR asymmetry (>=0.2)	**Both Eyes**				
	☐ Yes [1]				
	☐ No [2]				
	☐ Can not assess [3]				
Disc Haemorrhage	**Right Eye**			**Left Eye**	
	☐ Yes [1]			☐ Yes [1]	
	☐ No [2]			☐ No [2]	
	☐ Can not assess [3]			☐ Can not assess [3]	
Disc Notch	**Right Eye**			**Left Eye**	
	☐ Yes [1]			☐ Yes [1]	
	☐ No [2]			☐ No [2]	
	☐ Can not assess [3]			☐ Can not assess [3]	
Disc Atrophy	**Right Eye**			**Left Eye**	
	☐ Yes [1]			☐ Yes [1]	
	☐ No [2]			☐ No [2]	
	☐ Can not assess [3]			☐ Can not assess [3]	

Study ID ☐☐☐-☐☐

3.A. continued

Diabetic Retinopathy (Select **ONE** only)	**Right Eye**	**Left Eye**
	☐ No diabetic retinopathy	☐ No diabetic retinopathy
	☐ Non-proliferative	☐ Non-proliferative
	☐ Proliferative/end stage	☐ Proliferative/end stage
	☐ Cannot assess	☐ Cannot assess
Diabetic Maculopathy (Select **ONE** only)	☐ Diabetic Maculopathy	☐ Diabetic Maculopathy
	☐ No Diabetic Maculopathy	☐ No Diabetic Maculopathy
	☐ Cannot assess	☐ Cannot assess
Age Related Maculopathy (ARM)	**Right Eye**	**Left Eye**
	☐ No ARM [1]	☐ No ARM [1]
	☐ Drusen [2]	☐ Drusen [2]
	☐ Hypo/hyper pigmentation [3]	☐ Hypo/hyper pigmentation [3]
	☐ Can not assess [4]	☐ Can not assess [4]
Age Related Macular Degeneration (ARMD)	**Right Eye**	**Left Eye**
	☐ No ARMD	☐ No ARMD
	☐ Dry or Geographic	☐ Dry or Geographic
	☐ Wet/Neovascular/Disciform	☐ Wet/Neovascular/Disciform
	☐ Can not assess	☐ Can not assess
Other PSED Pathology	**Right Eye**	**Left Eye**
	☐ Yes	☐ Yes
	☐ No	☐ No
	☐ Can not assess	☐ Can not assess
If Yes - Specify (free text)	**R**	**L**

Study ID ☐☐☐-☐☐

3.B. Fundus Photography

Participant details entered on home screen	☐ Yes	☐ No
Participant Study ID Number	**XXX-XX**	☐☐☐-☐☐
Camera Failure?	☐ Yes	☐ No
ANTERIOR SEGMENT & LENS PHOTO *SIT PATIENT BACK SLIGHTLY ON CHIN REST (3cm)*		
Image clarity	**Right Eye**	**Left Eye**
	☐ Clear	☐ Clear
	☐ Hazy	☐ Hazy
	☐ No view	☐ No view
FUNDUS PHOTOGRAPH *AUTOMATIC MODE* *MANUAL IF UNABLE*		
Posterior Segment Image clarity	**Right Eye**	**Left Eye**
	☐ Clear	☐ Clear
	☐ Hazy	☐ Hazy
	☐ No view	☐ No view

Study ID ☐☐☐-☐☐

Participant information sheet – to be translated in to Kiswahili and read to participants

THE INCIDENCE AND PROGRESSION OF POSTERIOR SEGMENT EYE DISEASE IN NAKURU COUNTY IN RESIDENTS AGED 55 YEARS AND ABOVE

You are being invited to take part in a research study. Before you decide to take part, it is important for you to understand why the research is being done and what it will involve. I will read information to you about this study. Please ask me if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part

What is the purpose of the study?

In the world today there are about 39 million blind people. Approximately half of these people are blind due to cataract, making this the single largest cause of global blindness. In 2007/8 we undertook a survey to investigate how common eye diseases are among older people in Nakuru. This information helps us to plan health services more efficiently. We now want to follow-up the people we examined to see how quickly eye disease progresses and how often new eye disease occurs.

Why have I been chosen?

Every person who was randomly selected for the study 5 years ago (in 2007/2008) is being invited to take part again in the study so we can see what has happened to you over this time,

Do I have to take part?

No. It is up to you to decide whether or not to take part. If you decide to take part you will be asked to sign a consent form. If you decide to take part you are still free to withdraw at any time and without giving a reason.

What is involved in the study?

We will give you a very complete eye examination to look for any problem at the front and inside the eye using several machines. We will also check the pressure in your eye. Some of the examinations will involve contact with your eye. Some drops will be put in your eye so that you feel no pain. We will also put drops in your eyes to make the pupils as big as possible so we can see inside clearly. This will cause blurring of your near vision for a few hours afterwards and so you will not be able to drive or operate dangerous machinery for the rest of the day. The risks and likelihood of side-effects from this procedure is extremely small. We will also collect information about your history of diabetes, high blood pressure, eye diseases, smoking and alcohol all of which affect your eyes.

Your height, weight and blood pressure will be measured. A finger prick blood sample will be taken to check for diabetes, and a swab from the inside of your cheek will be taken to measure genetic material (DNA). This genetic material carries information for making up our bodies and is different in all people. Having DNA samples helps us to understand whether diseases run in the family. The results are unlikely to have any implications for you personally. We will store the DNA for future laboratory research that may be needed.

All information which is collected about you during the course of the research will be kept strictly confidential and your name will never be released.

Should we find that you could benefit from ant further eye treatment we will arrange an appointment for you to have treatment done at Nakuru eye unit. If you are found to be diabetic or have high blood pressure we will arrange for you be seen at the Nakuru provincial hospital. You will have to pay normal hospital fees for some of the treatment at the hospital. It is up to you to decide whether you would like to take up the offer of treatment or not.

Study ID ☐☐☐-☐☐

CONSENT FORM

The information sheet concerning this study has been read to me, and I understand what will be expected of me if I take part in this study.

My questions concerning this study have been answered by _____. I understand that participation in this study is voluntary. I also understand that I may withdraw from this study at any time without giving a reason and that this will not affect my normal care.

I agree to take part in this study.

I agree to have a sample of genetic material (DNA) taken: Yes/No

Name of study subject: _____

Signature or thumbprint _____

Witness _____

Date _____

* Witness: By signing in this column I warrant that I have read this form and the information form to the persons against whose names my signature appears. I am sure that each of these persons has understood what is required of him/her and has agreed to take part in the study.

Chapter 7. Six-Year Incidence of Blindness and Visual Impairment in Kenya: The Nakuru Eye Disease Cohort Study

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RESEARCH PAPER COVER SHEET

PLEASE NOTE THAT A COVER SHEET MUST BE COMPLETED FOR EACH RESEARCH PAPER INCLUDED IN A THESIS.

SECTION A – Student Details

Student	Andrew Bastawrous
Principal Supervisor	Hannah Kuper
Thesis Title	The Nakuru Eye Disease Cohort Study

If the Research Paper has previously been published please complete Section B, if not please move to Section C

SECTION B – Paper already published

Where was the work published?	Investigative Ophthalmology & Visual Science		
When was the work published?			
If the work was published prior to registration for your research degree, give a brief rationale for its inclusion			
Have you retained the copyright for the work?*		Was the work subject to academic peer review?	Yes

**If yes, please attach evidence of retention. If no, or if the work is being included in its published format, please attach evidence of permission from the copyright holder (publisher or other author) to include this work.*

SECTION C – Prepared for publication, but not yet published

Where is the work intended to be published?	
Please list the paper's authors in the intended authorship order:	
Stage of publication	

SECTION D – Multi-authored work

For multi-authored work, give full details of your role in the research included in the paper and in the preparation of the paper. (Attach a further sheet if necessary)	Study design, data collection, analysis, write up, review, overall lead.

Student Signature: _____ **Date:** 12, April 2017

Supervisor Signature: _____ **Date:** 12, April 2017

Six-Year Incidence of Blindness and Visual Impairment in Kenya: The Nakuru Eye Disease Cohort Study

Andrew Bastawrous,[1] Wanjiku Mathenge,[2] Kevin Wing,[3,4] Hillary Rono,[1,5] Michael Gichangi,[6] Helen A. Weiss,[7] David Macleod,[7] Allen Foster,[1] Matthew J. Burton,[1,8] and Hannah Kuper[1]

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Purpose. To describe the cumulative 6-year incidence of visual impairment (VI) and blindness in an adult Kenyan population. The Nakuru Posterior Segment Eye Disease Study is a population-based sample of 4414 participants aged ≥50 years, enrolled in 2007–2008. Of these, 2170 (50%) were reexamined in 2013–2014.

Methods. The World Health Organization (WHO) and US definitions were used to calculate presenting visual acuity classifications based on logMAR visual acuity tests at baseline and follow-up. Detailed ophthalmic and anthropometric examinations as well as a questionnaire, which included past medical and ophthalmic history, were used to assess risk factors for study participation and vision loss. Cumulative incidence of VI and blindness, and factors associated with these outcomes, were estimated. Inverse probability weighting was used to adjust for nonparticipation.

Results. Visual acuity measurements were available for 2164 (99.7%) participants. Using WHO definitions, the 6-year cumulative incidence of VI was 11.9% (95%CI [confidence interval]: 10.3–13.8%) and blindness was 1.51% (95%CI: 1.0–2.2%); using the US classification, the cumulative incidence of blindness was 2.70% (95%CI: 1.8–3.2%). Incidence of VI increased strongly with older age, and independently with being diabetic. There are an estimated 21 new cases of VI per year in people aged ≥50 years per 1000 people, of whom 3 are blind. Therefore in Kenya we estimate that there are 92,000 new cases of VI in people aged ≥50 years per year, of whom 11,600 are blind, out of a total population of approximately 4.3 million people aged 50 and above.

Conclusions. The incidence of VI and blindness in this older Kenyan population was considerably higher than in comparable studies worldwide. A continued effort to strengthen the eye health system is necessary to support the growing unmet need in an aging and growing population.

Keywords: Kenya, Africa, visual impairment, blindness, incidence, cohort, population-based

Global estimates based on recent population-based surveys suggest that approximately 191 to 285 million people live with visual impairment (VI; defined as visual acuity of <6/18 or <20/60 in the better eye), of whom 32 to 39 million people are bilaterally blind (visual acuity < 3/60 or < 20/400 in the better eye).[1,2] Overall, VI is ranked sixth in the global burden of disease in terms of disability-adjusted life-years (DALYs)[3] and is associated with increased mortality.[4,5] Despite a reduction in the prevalence of blindness in sub-Saharan Africa over the last two decades, the numbers with VI have risen due to an increase in population and longevity,[6] though data are sparse.

Longitudinal studies provide the opportunity to investigate the natural history of disease, which is essential to plan health services. However, despite a large body of data globally on the prevalence and causes of eye disease, data on incident visual loss from population-based cohorts are limited, due to prohibitive costs and complex logistical and planning challenges. Consequently, to date, no longitudinal, population-based studies of eye disease have been undertaken in sub-Saharan Africa, and there have been only a small number worldwide, predominantly in high-income settings.[7–10] Inferring data from high-income cohorts is not appropriate for low-income settings,

and data are required from low-income countries for effective planning of eye care services.

The aim of this study was to estimate the 6-year incidence and risk factors for incident VI and blindness (both bilateral and unilateral) in a cohort of adult Kenyans.

Materials and Methods

The methodology of the Nakuru Eye Disease Cohort Study has been reported in detail previously[11] and is summarized here.

Ethical Approval

The study adhered to the tenets of the Declaration of Helsinki and was approved by the Ethics Committee of London School of Hygiene and Tropical Medicine at both baseline and follow-up (LSHTM Ref. 6192). Baseline approval was provided by the Kenya Medical Research Institute Ethics Committee and by the African Medical and Research Foundation (AMREF) Ethics Committee, Kenya, for the follow-up (AMREF-ESRC P44/12). For both phases, approval was granted by the Rift Valley Provincial Medical Officer and the Nakuru District Medical Officer of Health. Approval was sought from the administrative heads in each cluster. Informed written (or thumbprint) consent was obtained from all participants after the objectives of the survey and the examination process were explained to those eligible in the local dialect, in the presence of a witness. Participants identified with eye conditions, or other health conditions, were referred to local services.

Baseline Study Population

The baseline population-based survey was conducted in 2007–2008. The sample size of 5000 participants aged ≥50 years was calculated based on an expected prevalence of visual acuity (VA) < 20/40 in the better eye due to posterior segment eye diseases (PSED, the primary outcome for the baseline survey) of 3.0% in this age group, precision of 0.5%, design effect of 1.5, and a response rate of 90%.

A total of 100 clusters each of 50 participants were selected with a probability proportional to the size of the population across Nakuru district. Households were selected within clusters using a modified compact segment sampling method.[12] An eligible individual was defined as someone aged ≥50 years living in the household for at least 3 months in the previous year. All participants were invited to undergo a comprehensive ophthalmic examination at a screening clinic (details below).

In total, 4381 (response rate 87.4%) participants underwent complete (ophthalmic and general) examination at baseline. Among those aged ≥50 years at baseline, the prevalence of blindness was 1.6% (95%CI [confidence interval]: 1.2–2.1%), and prevalence of VI was 13.6% (95%CI: 11.8–16.0%).[13]

Follow-up

Follow-up was conducted from January 2013 to March 2014.

Retracing at Follow-up: Advance Team. One week before the follow-up examination clinic was planned for a given cluster, a field officer studied the maps of the village including Global Positioning System (GPS) coordinates recorded at baseline and made phone contact with the village chief or guide to arrange the visit. At the planning visit, a list of study participants was given to the chief, and a local village guide was recruited to assist location of the study participants. At this visit, the examination site was established. Two days prior to the clinic, the field officer reminded chiefs of the visit by phone and notified them and the guide of the advance team's arrival.

On the day prior to the examination clinic, the advance team visited homes of baseline participants, confirmed their identity using National Identity cards, and invited them to attend the examination clinic the following day. All identified participants were also asked to help locate baseline participants who had not been found.

Examination Clinic. The following procedures were undertaken for all participants who attended the examination clinic at both baseline and follow-up, and further details are available elsewhere.[11] Procedures undertaken but not included in these analyses are not described in this report (e.g., visual field assessment).

Registration. On the examination day, the advance team confirmed the identity of participants against data from baseline (age, date of birth, name, and identity cards). In cases of uncertain identity, confirmation was made based on retinal examination verified by comparison of retinal photos with baseline photo ($n = 12$).

Visual Acuity Assessment. Presenting VA was measured using a back-illuminated modified logMAR reduced tumbling E chart (Sussex Vision, Inc., Rustington, UK),[14,15] which has been used in previous population-based studies.[16,17] Presenting VA was measured on all participants, that is, the patient's own correction was used if normally worn.

If the subject's vision was too poor to read any letters on the chart at 4 m, the subject was tested at 1 m, then as follows:

- Counting fingers (CF): ability to count fingers at 1-, 2-, or 3-m distance
- Hand motion (HM): ability to distinguish if a hand is moving or not in front of the patient's face
- Light perception (LP): ability to perceive any light
- No light perception (NLP): inability to see any light or total blindness

Those who did not read 24 letters (VA < 20/40) at 4 m were scheduled for correction and to undergo a repeat VA measurement with the correction in place unless the vision was worse than CF, in which case no correction was undertaken.

Anthropometry. A nurse performed and recorded measures of participants: height (Leicester Height Measure; Chasmors Ltd, London, UK); weight (Seca 761 Medical Class 4 Scales mechanical ground scale; Williams Medical Supplies, London, UK); waist and hip circumference (Chasmors Ltd WM02 Body Tape measure); and three measures of blood pressure (Omron Digital Automatic Blood Pressure Monitor Model HEM907; Omron, Hoofddorp, The Netherlands), each 10 minutes apart. In addition, at follow-up, bioimpedence (Tanita Segmental Body Composition Monitor; Tanita, Amsterdam, The Netherlands) was performed.

At baseline, capillary blood was taken from all participants for random blood glucose. Random blood glucose was also taken at follow-up with the addition of glycosylated hemoglobin (HbA1c) in all with a self-reported history of diabetes or random blood glucose of ≥7.0 mM, and a further 10% of nondiabetics (based on history and random blood glucose).

Interview. An interviewer performed a structured interview in the participant's preferred language covering demographic details; past medical and ocular history; known risk factors (e.g., smoking and tobacco consumption and alcohol intake); and socioeconomic status (e.g., job, housing conditions, ownership of material goods and livestock).[18]

Definitions and Statistical Analyses

All participants who had complete examinations at baseline who were not visually impaired or blind were considered "at risk" for incident VI or blindness, respectively. Follow-up status

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at 6 years was categorized as Found and examined; Found and not examined; Deceased; Moved away; or Unknown.

Statistical analysis was performed using STATA v13 (Stata Corp, College Station, TX, USA). All analysis accounted for the cluster survey design using Taylor linearized variance estimation to calculate standard errors.

Preparation of Cohort for Analysis

Pearson χ^2 tests corrected for the survey design were used to calculate P values in order to assess differences between participants seen and those lost to follow-up (LTFU), and between those known to have died and with unknown outcome status. $P < 0.1$ was considered to represent a statistically significant difference.

Those who were deceased were then excluded. Those followed up but without complete records for all covariates at baseline were also excluded.

An inverse probability weighting (IPW) model[19] was developed to allow estimation of cumulative incidence while accounting for those LTFU. Multivariable logistic regression was used to identify independent baseline covariates associated with LTFU. Covariates for which there was evidence of univariable association with the outcome ($P < 0.1$) were kept in a multivariable model. From this final model, the probability of being followed was estimated, based on the presence or absence of each of these baseline covariates. The inverse of this probability formed the weighting to be applied in order to account for those LTFU.

The final step was to remove those individuals LTFU from the cohort, so that all subsequent analysis would be performed on only those with complete outcome records, with IPW applied to account for those LTFU. A sensitivity analysis for this approach involved a complete records analysis (i.e., including only those people who had complete records for outcome and all variables in the analysis).

Estimation of Absolute and Relative Effects. The 6-year cumulative incidence of each outcome was calculated by dividing the number of events identified at 6-year follow-up by the number of people at risk at the beginning of follow-up; 95% confidence intervals were estimated assuming a Poisson distribution of events. This analysis was done for the population overall, and stratified by key covariates.

Age-adjusted risk ratios of the outcomes (VI and blindness, respectively) were estimated for each covariate using a Poisson regression model with robust error variance to allow for the clustered design and including IPW. For multivariable analysis, an initial model was fitted that included those variables associated with outcome in age-adjusted analysis (Wald P value < 0.05). A backward stepwise approach was applied to obtain a final multivariable model, removing variables with $P > 0.05$.

Definitions. Visual acuity: WHO definitions of VI and blindness were used throughout.[20] Monocular VI was defined as VA $<$ 6/18 (20/60) in either eye. Visual impairment was defined as a VA of $<$6/18 in the better eye. Monocular blindness was defined as a VA of $<$3/60 (20/400) in either eye. A person was considered to be blind if the VA in the better eye was $<$3/60. The definition of VI also includes those who were blind. An estimate of incident monocular and bilateral blindness using the US definition was also calculated. The US definition of monocular blindness is a Snellen acuity of $\leq$6/60 in either eye and $\leq$6/60 in the better eye for person blindness.[13]

Diabetes: Diabetes was defined as self-reported in the history, or random glucose $\geq$ 11.0 mM, or (3) HbA1c $\geq$ 7.0.

Socioeconomic status: A socioeconomic status (SES) score was developed based on information collected on job, housing conditions, and ownership of material goods and livestock, based on previous work in the same population.[18]

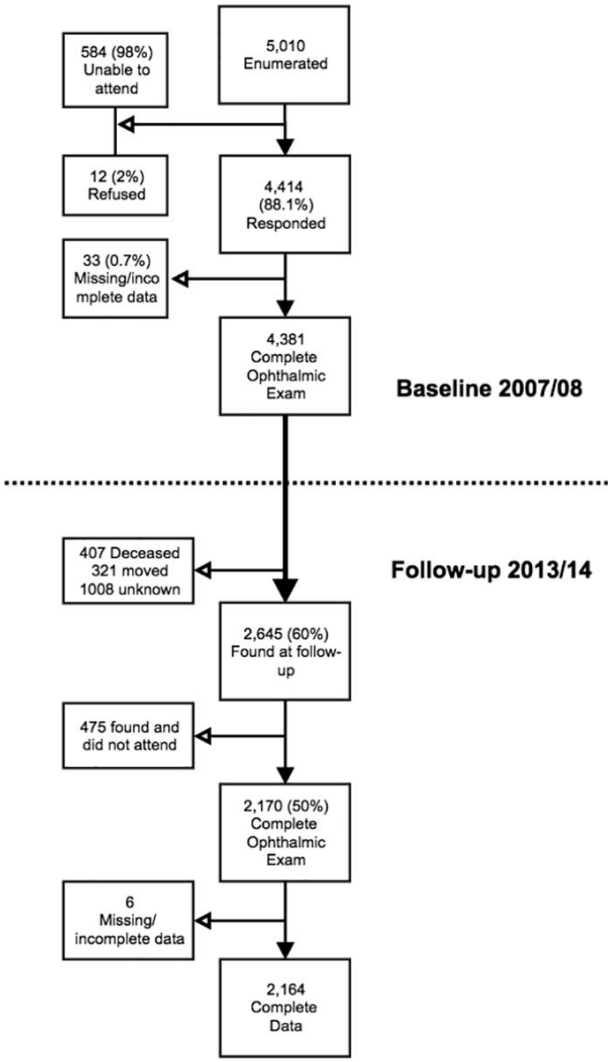

FIGURE. Flowchart of participants and nonparticipants.

Extrapolation of Data. Estimates of annual cumulative incidence were extrapolated to estimate the number of adults over the age of 50 with incident VI or blindness in Kenya each year. This was calculated by taking the 2015 population estimate from Kenya (Census Bureau of Kenya; Supplementary Table S2) by age category and sex and multiplying this by the age- and sex-specific estimates of annual cumulative incidence.

RESULTS

At baseline 4381 participants were examined (Fig.). Of these, 2645 (60%) were reidentified at the 6-year follow-up. The reasons for non–follow-up were migration (n = 321, 7%), deceased (n = 407, 10%), and unknown (n = 1008, 23%). Of the baseline participants, 2170 (50%) were reexamined. The large number of unknowns is thought to be due to mass displacement during the postelection violence in Kenya in 2007–2008.[21] Of the 2170 participants followed up, 2164 (99.7%) had complete data. Those with complete data available

Table 1. Baseline Characteristics in Nonblind Participants of the Nakuru Eye Disease Cohort Study: Participants and Nonparticipants ($n = 4310$)

		Participants	Nonparticipants or Not Included in Analysis			
Baseline Characteristics	**Missing Values**	**Followed Up, $n = 2140$, 49.7%**	**Not Followed Up Alive/ Unknown/DM Status Missing, $n = 1782$, 41.3%**	***P* Value***	**Deceased, $n = 388$, 9.0%**	***P* Value†**
Age, y, mean (SD)	0	62.5 (9.3)	62.3 (10.1)	0.743	70.8 (12.4)	<0.001
Sex, *n* (%)						
Female	0	1011 (47.2)	821 (46.1)	0.521	223 (57.5)	<0.001
Male		1129 (52.8)	961 (53.9)		165 (42.5)	
Vision status impaired, presenting <6/12 better eye, *n* (%)						
Normal	0	1983 (92.7)	1646 (92.4)	0.734	307 (79.1)	<0.001
Impaired		157 (7.3)	136 (7.6)		81 (20.9)	
Tribe, *n* (%)						
Kikuyu	0	1378 (64.4)	1064 (59.7)	<0.001	272 (70.1)	0.059
Kalenjin		530 (24.8)	365 (20.5)		84 (21.6)	
Other		232 (10.8)	353 (19.8)		32 (8.2)	
Education, *n* (%)						
None	11	192 (9.0)	203 (11.4)	0.030	25 (6.5)	0.001
Primary		668 (31.2)	568 (32.0)		163 (42.1)	
Secondary		1061 (49.6)	793 (44.7)		170 (43.9)	
Higher		217 (10.1)	210 (11.8)		29 (7.5)	
Residence, *n* (%)						
Rural	0	1612 (75.3)	995 (55.8)	<0.001	288 (74.2)	0.696
Urban		528 (24.7)	787 (44.2)		100 (25.8)	
SES quartile, *n* (%)						
Lower	31	499 (23.4)	432 (24.5)	0.008	125 (32.3)	0.004
Middle lower		587 (27.6)	394 (22.3)		91 (23.5)	
Middle upper		550 (25.8)	429 (24.3)		94 (24.3)	
Upper		493 (23.2)	508 (28.8)		77 (19.9)	

4381 individuals had a baseline measure of visual acuity. Of these, 71 were classified as blind, so the 4310 individuals who had a visual acuity measure and were nonblind contributed to this table. DM, diabetes mellitus.

* *P* value for association between the baseline characteristic and the odds of having a valid VI observation at follow-up, among all participants identified as nonblind at baseline and not known to be deceased at follow-up.

† *P* value for association between the baseline characteristic and the odds of dying during the follow-up period, among all participants identified as nonblind at baseline and either followed up or known to be deceased at follow-up (i.e., excluding the group who were not followed up).

were used in the model for missing data and adjustment of estimates. The mean follow-up time of all participants was 5.6 years (SD 0.6) and the median was 5.5 years (inter quartile range, 5.0–6.1), expressed as a "6-year cumulative incidence" from here on. The Supplementary Figure includes the visual status of participants at both time points in the cohort study.

Table 1 provides the baseline characteristics of participants who were reexamined at follow-up and those who were LTFU. In comparison to participants, there was strong evidence that those who had died during follow-up were older, were more likely to be male, and had lower education and SES. Compared with participants seen, those LTFU were less likely to be Kikuyu or Kalenjin speakers, had lower levels of education, were more likely to be from urban areas, and had higher SES.

In those followed up, the prevalence of VI was higher at follow-up (23%) than at baseline (13%), suggesting an overall shift toward VI in this aging cohort (Table 2). Of the 45 blind at follow-up, the majority were incident cases ($n = 29$, 64%). Eight of 24 blind persons at baseline were no longer blind at follow-up, having received treatment in the interim period; however, only 2 had achieved normal vision (Table 2).

Incidence of Blindness and Visual Impairment

Of the 2164 participants with complete follow-up data, 24 were blind at baseline and were therefore excluded from the group considered at risk of becoming blind. We analyzed 2140 subjects at risk for incident blindness, of whom 29 participants (1.36%, 95%CI: 0.9–1.9%) were blind at the follow-up visit (Table 3). All subsequent results presented here have been calculated based on the at-risk population and take account of clustering, and also account for missing data via IPW, unless otherwise stated.

The cumulative incidence, in participants aged 50 years and over, of WHO-defined bilateral and unilateral VI was 119.4/1000 (95%CI 103.1–137.9) and 228.0/1000 (95%CI 206.0–251.6), respectively (Table 3). The cumulative incidence of WHO-defined bilateral and unilateral blindness was 15.1/1000 (95%CI 10.4–21.7) and 54.6/1000 (95%CI 43.7–68.0), respectively. Unweighted estimates using only those participants with complete records of incidence were similar: WHO-defined (Supplementary Table S3) bilateral and unilateral VI was 118.0/1000 (95%CI 102.0–136.2) and 226.6/1000 (95%CI 204.8–250.0), respectively (Supplementary Table S1), with estimates

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Table 2. Change in Presenting Visual Acuity Category From Baseline to Follow-Up in Cohort With Visual Acuity Data From Both Time Points (n = 2164)

	Follow-Up					
Baseline	**≥6/12**	**<6/12–6/18**	**<6/18–6/60**	**<6/60–3/60**	**<3/60**	**Total**
≥6/12	1474	227	166	4	10	1881, 86.9%
<6/12–6/18	18	30	51	1	2	102, 4.7%
<6/18–6/60	15	22	82	16	15	150, 6.9%
<6/60–3/60	0	0	5	0	2	7, 0.3%
<3/60	2	1	4	1	16	24, 1.1%
Total	1509, 69.7%	280, 12.9%	308, 14.2%	22, 1.0%	45, 2.0%	2164, 100%

2164 individuals had both a baseline measure of visual acuity and a follow-up measure of visual acuity. All are included in this table. Visual acuity categories are presenting visual acuity in the better of eye of the individual.

of blindness being slightly lower at 13.6/1000 (95%CI 9.5–19.4).

The cumulative incidence using the US definitions of blindness was estimated to enable comparison with other cohorts, and was higher than for WHO estimates (Table 3). All further analyses are based on WHO definitions.

There was strong evidence of an increase in 6-year cumulative incidence of VI and blindness by age (Table 4). Overall differences in sex across all age categories were not evident; however, a significant difference was found between male and females aged ≥80 years for cumulative incidence of both VI and blindness.

Extrapolations based on recent census data were used to calculate the number of individuals aged ≥50, by age and sex, estimated to become visually impaired or blind in Kenya each year (Table 5, Supplementary Table S4). There are an estimated 21 new cases of VI in people aged ≥50 years per 1000 total population per year, of whom 3 (2.7) are blind. Therefore in Kenya we estimate that there are 92,000 new cases of VI per year in people aged ≥50 years, of whom 11,600 are blind, out of a total population of approximately 4.3 million people aged ≥50 (Supplementary Table S5).

Data from other similar populations indicate that 85% of blindness prevalence is among those aged ≥50 years.[22] Assuming that the relative incidence of blindness in the under- and over-50s is comparable to the prevalence (i.e., 85% of incidence is also in the over-50s), extrapolating to all ages, we estimate that there are 1.66 new cases of blindness per 1000 per year in all ages in Kenya, approximately 76,000 new cases annually out of a total population of 46 million.

Multivariable analysis for incident bilateral blindness and VI, respectively, showed only diabetes and increasing age to be associated (Table 6). However, low numbers of incident cases of blindness and wide confidence intervals make drawing conclusions limited for this group. There was no evidence of an association with all other risk factors.

Discussion

There are few longitudinal population-based studies describing the incidence of blindness and VI worldwide, and data from sub-Saharan Africa are particularly sparse (Table 7). The data build on our previously reported population-based estimates of prevalence in the same population.[13]

We found that the annual incidence of blindness in those aged 50 years and over was 2.2 per 1000 people per year using the WHO definition (VA < 20/400 Snellen in the better-seeing eye) and 4.3 per 1000 for the US definition (VA ≤ 20/200 in the better-seeing eye). The annual incidence of VI (VA < 6/18 Snellen in the better-seeing eye) was 20.9 per 1000 people per year. These estimates are substantially higher annual incidence rates of VI and blindness when compared with other cohort studies (Table 7). It should be noted that comparable studies had varying follow-up periods and thus comparison is made based on annual incidence.

As expected, the incidence of VI and blindness increased significantly with age, as seen in all previous comparable cohort studies. This reflects age-related changes to the crystalline lens and age-related retinal and nerve diseases.

Table 3. Six-Year Adjusted Cumulative Incidence of Unilateral and Bilateral Visual Impairment by WHO and US Criteria Among the Nakuru Eye Disease Cohort Study Participants

	WHO Criteria			US Criteria	
Incidence of	**Incident Cases/ At Risk Cases**	**Cumulative Incidence, n per 1000 of Population (95% CI)**	**Cumulative Incidence per Million of Population, n per 1 Million of Population (95% CI)**	**Incident Cases/ At Risk Cases**	**Cumulative Incidence, n per 1000 of Population (95% CI)**
Bilateral blindness	29/2140	15.1 (10.4–21.7)	15,100 (10,400–21,700)	53/2122	25.9 (19.4–34.4)
Bilateral visual impairment	234/1983	119.4 (103.1–137.9)	119,400 (103,100–137,900)	–	–
Unilateral blindness	111/1984	54.6 (43.7–68.0)	54,600 (43,700–68,000)	154/1937	79.9 (68.2–93.4)
Unilateral visual impairment	390/1721	228.0 (206.0–251.6)	228,000 (206,000–251,600)	–	–

WHO definition: blind, Snellen acuity < 3/60 (<20/400); visually impaired, Snellen acuity < 6/12 (<20/40). US definition: blind, Snellen acuity ≤ 6/60. Cumulative incidence adjusted for missing data. 2164 individuals had VA measurements at baseline and follow-up, but 24 of these had WHO bilateral blindness at baseline, hence 2164 − 24 = 2140 at risk; 181 had WHO bilateral visual impairment at baseline, hence 2164 − 181 = 1983 at risk; 180 had WHO unilateral blindness at baseline, hence 2164 − 180 = 1984 at risk; 443 had WHO unilateral visual impairment at baseline, hence 2164 − 443 = 1721 at risk; 42 had US-defined bilateral blindness, hence 2164 − 42 = 2122 at risk; 227 had US-defined unilateral blindness, hence 2164 − 227 = 1937 at risk.

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Table 4. Age- and Sex-Specific 6-Year Adjusted Cumulative Incidence of Visual Impairment and Blindness by WHO Definition Among the Nakuru Eye Disease Cohort Study Participants

	Male		Female		Overall	
Age Group, Years	*n*, Cases/ At Risk	Risk per 1000/6 Years (95%CI)	*n*	Risk per 1000/6 Years (95%CI)	*n*	Risk per 1000/6 Years (95%CI)
Visual impairment, <6/18 better eye						
50–59	27/402	66.5 (44.2–99.0)	30/556	53.3 (36.3–77.5)	57/958	58.8 (44.4–77.6)
60–69	35/328	110.4 (77.6–154.7)	37/314	119.8 (87.2–162.3)	72/642	115.1 (90.2–145.8)
70–79	34/156	218.4 (152.8–302.3)	39/137	283.8 (213.1–367.1)	73/293	249.9 (204.1–302.0)
80+	13/43	308.5 (183.6–469.5)	19/47	411.4 (268.9–570.5)	32/90	363.2 (270.6–467.3)
All age groups	109/929	118.6 (94.6–147.5)	125/1054	120.1 (100.8–142.6)	234/1983	119.4 (103.1–137.9)
Blindness, <3/60 better eye						
50–59	1/407	2.3 (0.3–16.5)	0/568	–	1/975	0.9 (0.1–6.9)
60–69	5/353	14.4 (6.0–34.3)	3/337	9.8 (3.0–32.3)	8/690	12.1 (5.9–24.7)
70–79	4/183	28.6 (10.1–77.8)	4/157	24.0 (9.4–59.7)	8/340	26.4 (13.1–52.4)
80+	3/68	58.4 (17.4–178.7)	9/67	129.7 (68.6–231.6)	12/135	94.6 (53.7–161.5)
All age groups	13/1011	15.2 (8.4–27.4)	16/1129	15.0 (9.3–24.1)	29/2140	15.1 (10.4–21.7)

The disease-specific incidence rates will be presented and discussed in separate reports.

One previous study from Uganda assessed the incidence of VI and blindness in an African population from a population-based cohort that was established to assess the dynamics of human immunodeficiency virus (HIV) infection through annual censuses and serologic surveys,[29] and incorporated an assessment of vision at two time points. The sample was a general population cohort and not designed specifically for eye disease, measuring only VA (modified Snellen chart).[30] Only one case of incident bilateral blindness was reported and 21 cases of incident VI in the study sample (aged 13 and above), providing an age-standardized incidence rate of bilateral VI of 13.2 persons per 1000 persons per year (in a different age group from that presented from this population).[31] In comparison, this study estimated an incidence of VI at 20.9 persons per 1000 per year.

There are data from comparable population-based studies of eye disease worldwide (Table 7). There are some variations in the age group considered for inclusion, although the majority sampled those 40 or 50 years and above. Most studies presented incident data using the WHO and US definitions of VI or blindness, but some included only one definition, limiting comparability across studies. The incidence of bilateral VI in the Nakuru Eye Disease Cohort Study was found to be higher than anywhere else in the world. The annual incidence rate (persons per 1000 per year) for the majority of studies (eight) was between 0.2 and 0.9 (US classifications) and 0.1 and 0.5 (WHO classifications).[8–10,23,25–28] Only two studies were higher, at 1.1 (US) and 2.1 (WHO) for the Barbados Eye Study[24] and 1.2 (US) and 2.4 (WHO) for the Nakuru Eye Disease Cohort Study, respectively.

The high incidence in this study most likely reflects a combination of low access to ophthalmic services and health services in general[32]; there was only one ophthalmologist in the region of the study for a population of approximately 1.6 million people. Other explanations include environmental risk factors including geography, diet, ethnic origin, and ultraviolet light exposure. Other barriers to eye care provision in the region include a low awareness of treatable sight loss, available services that are unaffordable and far away, and fear of treatment.

The data in this study indicated that of 29 new cases of blindness at follow-up, 12 had VA of 6/18 or better, and 17 were worse than 6/18 (see Table 2). Of the 24 who were blind at baseline, 16 were still blind at follow-up. Further analysis will disaggregate incident VI and blindness by cause, enabling

Table 5. Extrapolated Number of Adults per Year, Aged 50 Years and Over, in Kenya With New Visual Impairment and Blindness Based on Weighted Incidence Data and Estimates of the Population in Kenya by Age Group in 2015

	Male			Female			Overall		
Age Group, Years	Extrapolated Number	Lower, 95%CI	Upper, 95%CI	Extrapolated Number	Lower, 95%CI	Upper, 95%CI	Extrapolated Number	Lower, 95%CI	Upper, 95%CI
Visual impairment									
50–59	11,480	7,620	17,080	10,130	6,910	14,740	21,340	16,090	28,160
60–69	9,710	6,830	13,600	13,030	9,490	17,660	22,670	17,760	28,710
70–79	7,700	5,380	10,650	13,670	10,260	17,680	20,720	16,920	25,040
80+	2,200	1,310	3,340	4,470	2,920	6,200	6,490	4,830	8,350
All age groups	34,550	27,580	43,000	42,230	35,430	50,120	76,740	66,240	88,650
Blindness, <3/60 better eye									
50–59	400	50	2,890	–	–	–	350	50	2,550
60–69	1,350	560	3,190	1,160	350	3,810	2,560	1,250	5,200
70–79	1,200	430	3,280	1,340	530	3,330	2,580	1,280	5,120
80+	680	200	2,070	2,190	1,160	3,900	2,680	1,520	4,580
All age groups	4,870	2,690	8,780	5,740	3,550	9,240	10610	7,340	15,300

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Table 6. Age-Adjusted and Multivariable Analysis of a Number of Baseline Covariables and Incident Visual Impairment and Blindness in the Nakuru Eye Disease Cohort Study

	Bilateral Visual Impairment, At Risk Sample, $n = 1983$					Bilateral Blindness, At Risk Sample, $n = 2140$				
	No. at Risk of Bilateral VI	Incident VI	Risk per 1000/6 Years (95%CI)	Age-Adjusted Risk Ratio	Multivariable Risk Ratio (95%CI)*	No. at Risk of Bilateral Blindness	Incident Blindness	Risk per 1000/6 Years (95%CI)	Age-Adjusted Risk Ratio (95%CI)	Multivariable Risk Ratio (95%CI)*
Age										
50–59	958	57	58.8 (44.4–77.6)	Reference	Reference	975	1	0.9 (0.1–6.9)	Reference	Reference
60–69	642	72	115.1 (90.2–145.8)	2.0 (1.4–2.8)	1.8 (1.3–2.6)	690	8	12.1 (5.9–24.7)	12.8 (1.5–108.2)	12.8 (1.5–108.2)
70–79	293	73	249.9 (204.1–302.0)	4.2 (3.0–5.9)	3.7 (2.6–5.1)	340	8	26.4 (13.1–52.4)	27.9 (3.3–232.9)	27.9 (3.3–232.9)
80+	90	32	363.2 (270.6–467.3)	6.2 (4.1–9.3)	5.0 (3.3–7.6)	135	12	94.6 (53.7–161.5)	100.0 (12.5–801.0)	100.0 (12.5–801.0)
Sex										
Male	929	109	118.6 (94.6–147.5)	Reference		1011	13	15.2 (8.4–27.4)	Reference	
Female	1054	125	120.1 (100.8–142.6)	1.1 (0.9–1.4)		1129	16	15.0 (9.3–24.1)	1.1 (0.5–2.5)	
Location										
Rural	1480	193	135.0 (114.5–158.5)	Reference		1612	22	14.9 (9.9–22.5)	Reference	
Urban	503	41	89.6 (65.8–120.9)	0.9 (0.6–1.2)		528	7	15.4 (7.2–32.7)	1.6 (0.7–3.7)	
SES quartile										
Lower	436	86	203.2 (171.8–238.7)	Reference	Reference	499	11	25.7 (13.8–47.4)	Reference	
Lower middle	547	66	122.0 (93.0–158.4)	0.6 (0.5–0.8)	0.6 (0.5–0.8)	587	7	13.7 (6.5–28.5)	0.6 (0.2–1.7)	
Upper middle	518	51	99.0 (73.9–131.5)	0.6 (0.4–0.8)	0.6 (0.4–0.8)	550	5	8.3 (2.9–23.0)	0.5 (0.2–1.7)	
Upper	471	29	65.4 (46.8–90.8)	0.4 (0.3–0.6)	0.4 (0.3–0.6)	493	6	13.2 (5.3–32.3)	1.1 (0.4–3.2)	
Smoker										
Never	1378	162	120.4 (102.9–140.4)	Reference		1488	23	16.4 (11.1–24.2)	Reference	
Former	150	16	110.9 (69.7–172.1)	0.9 (0.6–1.4)		163	3	24.6 (7.4–78.3)	1.7 (0.5–5.6)	
Current	454	56	119.3 (87.3–161.0)	0.9 (0.7–1.3)		488	3	7.0 (2.2–21.9)	0.4 (0.1–1.1)	
Hypertension										
No	1030	111	106.6 (86.0–131.5)	Reference		1109	11	11.2 (6.3–19.8)	Reference	
Yes	944	122	133.5 (112.1–158.4)	1.1 (0.8–1.4)		1021	17	18.3 (11.4–29.3)	1.2 (0.6–2.4)	
Diabetic										
No	1881	214	114.6 (97.3–134.4)	Reference	Reference	2029	24	13.1 (8.8–19.6)	Reference	Reference
Yes	100	20	204.2 (132.2–301.6)	1.6 (1.0–2.5)	1.9 (1.2–3.0)	109	5	48.7 (19.7–115.8)	2.8 (1.0–7.9)	2.8 (1.0–7.9)
Alcohol										
Never	834	81	99.7 (80.3–123.3)	Reference		872	12	13.5 (7.5–24.0)	Reference	
Former	851	107	125.3 (103.2–151.3)	1.0 (0.8–1.4)		926	11	14.4 (7.9–26.0)	0.7 (0.3–1.7)	
Current	293	45	157.7 (113.0–215.8)	1.5 (1.0–2.0)		337	6	20.8 (8.3–51.2)	1.1 (0.4–3.2)	
Ethnic group										
Kikuyu	1292	142	111.8 (93.1–133.7)	Reference		1378	18	14.6 (8.9–24.0)	Reference	
Kalenjin	472	68	146.8 (113.8–187.4)	1.4 (1.0–1.9)		530	9	20.4 (10.7–38.5)	1.5 (0.7–3.2)	
Other	219	24	111.7 (70.2–173.3)	1.5 (0.9–2.3)		232	2	8.9 (2.1–36.7)	1.2 (0.2–5.4)	
Education level										
No education	188	9	49.8 (24.4–99.2)	Reference		192	2	11.6 (2.7–47.6)	Reference	
Primary	577	108	192.7 (162.3–227.4)	2.2 (1.1–4.3)		668	17	28.3 (17.3–46.0)	0.6 (0.1,2.7)	
Secondary	1004	107	105.6 (86.2–128.7)	1.6 (0.8–3.2)		1061	10	10.5 (5.3–20.8)	0.4 (0.1–2.3)	
College/Univ	212	10	55.1 (28.3–104.6)	1.2 (0.5–2.9)		217	0	–	–	

* For multivariable analysis, an initial model was fitted that included those variables shown to be associated with outcome in age-adjusted analysis (using a Wald test threshold P value of < 0.05 to indicate association). A backward stepwise approach was then applied in order to obtain a final multivariable model, removing variables with $P > 0.05$ one by one.

Table 7. Estimates of Incidence of Blindness From Comparative Population-Based Studies of Eye Disease

Study	Location	Year Commenced	Age at Baseline	Years of Follow-Up	No. of Participants	Cumulative Blindness Incidence (Definition Used)	Annual Blind Incidence Rate (Persons/1000/Year)	Cumulative Visual Impairment Incidence (Persons/1000/Year)	Annual Visual Impairment Incidence Rate (Persons/1000/Year)	Reference
Beaver Dam Eye Study	United States	1988		Baseline	4926					23
				5	3721					
				10	2962					
				15	2375	0.8% (US)	0.5	8.0%	5.0	
				20	1913	–	–	–	–	
Blue Mountains Eye Study	Australia	1992		Baseline	3654					8
				5	2335					
				10	1952					
				15	1149	0.9% (US)	0.6	5.2%	3.5	
Barbados Eye Study	Barbados	1987	40+	Baseline	4631					24
				4	3427	1.0% (WHO)	1.1	6.0%	6.7	
				9	2793	2.1% (US)	(2.3)	(9.0%)	(10.0)	
Reykjavik Eye Study	Iceland	1996	50+	Baseline	1045	0.35% (WHO)	0.7	1.1%	2.2	9
				5	846	0.95% (US)	(1.9)	(3.49%)	(7.0)	
Los Angeles Latino Eye Study	United States	2000	40+	Baseline	6357					10
				4	4658	0.3% (US)	0.8	2.9%	7.3	
Chennai Eye Disease Study	India	2001	40+	Baseline	7774					25
				6	4419	0.48% (WHO)	0.8	–	–	
Liwan Eye Study	China	2003	50+	Baseline	1405	0.33% (WHO)	0.7	5.4%	10.8	26
				5	1232	1.42% (US)	(2.8)	(9.9%)	(19.8)	
Beijing Eye Study	China	2001	40+	Baseline	4438	0.1% (WHO)	0.2	1.7%	3.4	27
				5	3251	0.2% (US)	(0.4)	(3.8%)	(7.6)	
Priverno Eye Study	Italy		45–69	Baseline	860					28
				7	619	0.2% (WHO)	0.3	1.3%	1.9	
Nakuru Eye Disease Cohort Study	Kenya	2007	50+	Baseline	4414	1.51% (WHO)	2.7	11.9%	21.3	This paper
				6	2171	2.59% (US)	(4.6)			

further data to support planning (e.g., estimation of need for cataract surgery).

Strengths of the study include the following characteristics: a representative population-based sample in an area of ethnic, socioeconomic, and educational diversity; a large sample size; comprehensive assessment of risk factors; high-quality assessment of vision; and utilization of the same tools at baseline and follow-up. The methodology used to assess ophthalmic disease was consistent with studies performed in well-developed health systems in high-income countries such as the United States[23] and Australia,[8] with use of the latest available equipment,[11] thus making the data highly comparable to those in other population-based cohort studies of eye disease.

The major limitation of this study was low participation rate (50%) at 6 years; however, having the baseline characteristics of nonparticipants is a strength that enabled weighting to ensure better estimates of cumulative incidence. This loss to follow-up may have led to an under- or overestimation of incident VI and blindness, depending on the general characteristics of the nonrespondents. The predominant risk factor for incident VI or blindness was age; and given that this was closely matched between participants and nonparticipants (62.7 years [SD 9.4] and 62.5 years [SD 10.4], respectively), the estimates are likely to be an acceptable reflection. This assessment is further supported in that minimal changes were apparent after adjusting estimates for missing data (Supplementary Table S1).

Reasons for the low participation included ethnic violence and displacement of large numbers of people in the study sample area. Postelection violence in 2007 and 2008 led to up to 600,000 people being internally displaced and 1300 fatalities.[21] In a number of study clusters, entire ethnic groups present at baseline were no longer available or traceable. Great efforts were made to locate individuals. Further limitations include restricting the inclusion criteria at baseline to those 50 years and above, thereby reducing the generalizability of our results to the entire population. This is, however, comparable to the majority of population-based studies of eye disease that restrict inclusion to 40 or 50 years and above (Table 7). Furthermore, the majority of prevalent and incident vision loss is in this age group, making the sample size feasible.[22] The definition of blindness and VI in this study did not include peripheral vision loss and was based solely on presenting central logMAR VA. This potentially underestimates the incident VI and blindness (particularly from glaucoma) when compared to studies that include these criteria.

Our results suggest that there are 86,000 new cases of VI in people aged $\geq$50 years per year in Kenya, of whom 8100 are blind. Recent estimates suggest that there are 86 ophthalmologists in Kenya[33] for a population of approximately 45 million, with the majority (50%) being based in the capital city of Nairobi. This leaves 92% of the population (approximately 40 million people) being served by 43 ophthalmologists. Overall, Kenya is better resourced than many other African countries in terms of human resources, despite still being well below recommended targets.[34] Continued effort to strengthen the eye health system is necessary to support the growing unmet need of this aging and growing population.

In conclusion, the incidence of VI and blindness in this adult Kenyan population was considerably higher than in comparable studies worldwide. Further analyses on the causes of incident blindness will help in setting priorities for preventing avoidable blindness in this population.

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Supplementary Material

Data cleaning and management

All raw data collected during the fieldwork was imported from Excel into STATA and the variables and categories of the collected variables were labelled appropriately, before checking for missing data and likely input errors. Any issues identified were discussed within the study team, in order to identify whether the issue was expected based upon the study design and data collection approach used in the field. Unexpected issues were resolved by checking the source data. Outcome variables were then generated, based on the collected field data. These included blindness and visual impairment (at follow-up) outcome variables per person and per eye (i.e. monocular) according to the WHO (for both blind and visual impairment) and the U.S. (for blind only) standards (see Supplementary Table S1).

Co-variate (recorded at baseline) variables were then set up for age, gender, education, diabetes, socioeconomic status (SES) and hypertension. A categorical age variable was created (10 year age categories from 50 onwards). Education was defined as none, primary, secondary and higher. SES included lower, middle lower, middle upper and upper quartile categories. All other co-variates were setup as binary variables (i.e. male/female or no/yes, with male and no as baseline categories). A dedicated cohort analysis dataset was then created that contained the unique study ID for each individual, the village of residence (which defined the cluster in subsequent analysis), the individual's follow up status (i.e. participant vs non-participant), whether the person died or not, the outcome variables and the covariates.

Table S1. Baseline Characteristics in Nakuru Eye Disease Cohort Study: Participants and Non-participants

		Participants	**Non-participants**			
Baseline Characteristics		*(n=2,171, 49.2%)*	*Alive/Unknown n=1,834, (41.5%)*	*p-value*	*Deceased (n=409, 9.3%)*	*p-value*
Age (yrs), mean +/- SD		62.7 (9.4)	62.5 (10.4)	0.50	71.6 (12.8)	<0.001
Male % (n)		47.3% (1,026)	46.4% (851)	0.59	57.7% (236)	<0.001
Vision status	Normal (≥6/12 both eyes)	91.6% (1,988)	91.0% (1,641)	0.47	75.4 % (307)	<0.001
	Impaired (<6/12 better eye)	8.4% (182)	9.0% (163)		24.6% (100)	
Tribe % (n)	Kikuyu	64.2% (1,393)	59.1% (1,084)	<0.001	69.2% (283)	0.10
	Kalenjin	25.1% (544)	20.6% (378)		22.7%(93)	
	Other	10.8% (234)	20.3% (372)		8.1% (33)	
Education % (n) [a]	None	8.9% (193)	11.1% (204)	<0.001	6.4% (26)	<0.001
	Primary	31.7% (689)	32.0% (586)		43.8% (179)	
	Secondary	49.3% (1,070)	43.9% (805)		42.5% (174)	
	Higher	10.0% (217)	11.7% (215)		7.1% (29)	
Urban % (n)		24.5% (532)	44.1% (808)	<0.001	25.9% (106)	0.54
SES Quartile % (n)[b]	Lower	23.8% (517)	23.9% (439)	<0.001	33.3% (136)	0.002
	Middle lower	27.2% (591)	22.0% (404)		23.5% (96)	
	Middle upper	25.7% (557)	23.9% (438)		23.7% (97)	
	Upper	22.8% (495)	28.2% (517)		19.3% (79)	

P values represent the difference between participants and non-participants (deceased and

alive/unknown), results of a chi-squared test of overall association of the variable.

a. Missing data on 27 participants, b. missing data on 48 participants

Note 24 participants followed up were blind at baseline, therefore n= 2,160 – 24 = 2,136

Table S2. Estimates of Population of Kenya in 2015			
Age	**Both Sexes Population**	**Male Population**	**Female Population**
All ages	45,925,301	22,907,500	23,017,801
50-59	2,231,660	1,061,476	1,170,184
60-69	1,278,899	565,224	713,675
70-79	594,118	258,604	335,514
80+	187,131	78,468	108,663
50+	4,291,808	1,963,772	2,328,036

Table S3. Six-Year unweighted Cumulative Incidence of Unilateral and Bilateral Visual Impairment by World Health Organization and United States Criteria among the Nakuru Eye Disease Cohort Study Participants.

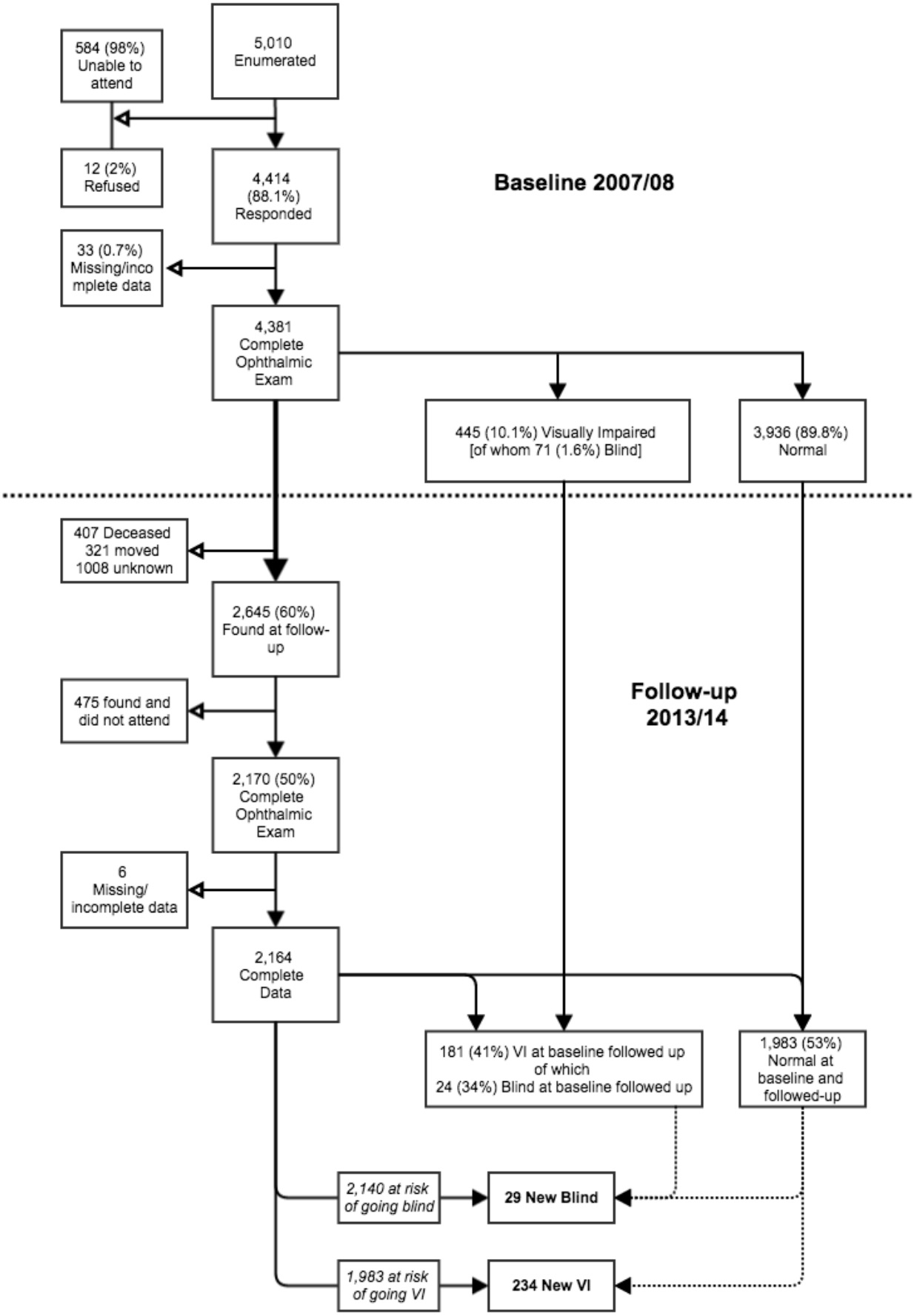
	WHO criteria			US criteria	
Incidence of	Incident cases / At risk cases	Cumulative incidence (n / per 1000 of population, 95% CI)	Cumulative incidence per million of population (n / per 1m of population, 95% CI)	Incident cases / At risk cases	Cumulative incidence (n / per 1000 of population, 95% CI)
Bilateral blindness	29 / 2140	13.6(9.5,19.4)	13,600 (9,500-19,400)	53 / 2122	25.0(18.9,33.0)
Bilateral Visual Impairment	234 / 1983	118.0(102.0,136.2)	118,000 (102,000-136,200)	-	-
Unilateral blindness	111 / 1984	55.9(45.3,68.8)	55,900 (45,300-68,800)	154 / 1937	79.5(68.2,92.4)
Unilateral Visual Impairment	390 / 1721	226.6(204.8,250.0)	226,600 (204,800-250,000)	-	-

Table S4. Age-Gender–Specific 6-Year unweighted cumulative incidence of Visual Impairment and Blindness by World Health Organization definition among the Nakuru

	Male		Female		Overall	
Age Group (years)	n (Cases / at risk)	Risk per 1,000/6yrs (95%CI)	n	Risk per 1,000/6yrs (95%CI)	n	Risk per 1,000/6yrs (95%CI)
Visual Impairment (<6/18 better eye)						
50-59	27 / 402	67.2(47.5,94.1)	30 / 556	54.0(37.7,76.6)	57 / 958	59.5(46.1,76.4)
60-69	35 / 328	106.7(74.9,149.9)	37 / 314	117.8(85.4,160.5)	72 / 642	112.1(87.2,143.1)
70-79	34 / 156	217.9(151.6,303.0)	39 / 137	284.7(212.2,370.3)	73 / 293	249.1(202.8,302.0)
80+	13 / 43	302.3(183.8,454.8)	19 / 47	404.3(264.1,562.0)	32 / 90	355.6(264.7,458.2)
All age groups	109 / 929	117.3(94.3,145.0)	125 / 1054	118.6(99.3,141.1)	234 / 1983	118.0(102.0,136.2)
Blindness (<3/60 better eye)						
50-59	1 / 407	2.5(0.3,17.7)	0 / 568	-	1 / 975	1.0(0.1,7.5)
60-69	5 / 353	14.2(6.0,33.2)	3 / 337	8.9(2.9,27.4)	8 / 690	11.6(5.8,23.0)
70-79	4 / 183	21.9(8.1,57.6)	4 / 157	25.5(10.1,62.7)	8 / 340	23.5(12.1,45.2)
80+	3 / 68	44.1(13.7,133.0)	9 / 67	134.3(73.1,233.9)	12 / 135	88.9(50.2,152.6)
All age groups	13 / 1011	12.9(7.3,22.4)	16 / 1129	14.2(8.9,22.5)	29 / 2140	13.6(9.5,19.4)

Table S5. Extrapolated number of new adults per year, aged 50 years and over in Kenya with visual impairment and blindness based on unweighted incidence data and estimates of the population in Kenya by age group in 2015.

	Male			**Female**			**Overall**		
Age Group (years)	Extrapolated number	Lower (95%CI)	Upper (95%CI)	Extrapolated number	Lower (95%CI)	Upper (95%CI)	Extrapolated number	Lower (95%CI)	Upper (95%CI)
Visual Impairment									
50-59	11590	8200	16230	10260	7180	14560	21580	16740	27710
60-69	9380	6580	13180	12820	9290	17450	22090	17180	28180
70-79	7680	5340	10680	13710	10220	17840	20660	16820	25040
80+	2150	1310	3240	4390	2870	6110	6350	4730	8190
All age groups	34190	27500	42260	41680	34880	49600	75830	65530	87510
Blindness (<3/60 better eye)									
50-59	430	60	3110	#VALUE!	#VALUE!	#VALUE!	380	50	2760
60-69	1320	560	3100	1050	340	3230	2450	1230	4860
70-79	920	340	2430	1420	560	3500	2300	1180	4420
80+	510	160	1540	2260	1230	3940	2520	1420	4330
All age groups	4120	2350	7190	5430	3410	8630	9540	6660	13640


5,010
Enumerated
584 (98%)
Unable to
attend
12 (2%)
Refused
4,414
(88.1%)
Responded
33 (0.7%)
Missing/inco
mplete data
4,381
Complete
Ophthalmic
Exam
445 (10.1%) Visually Impaired
[of whom 71 (1.6%) Blind]
3,936 (89.8%)
Normal
Baseline 2007/08
407 Deceased
321 moved
1008 unknown
2,645 (60%)
Found at follow-
up
475 found and
did not attend
2,170 (50%)
Complete
Ophthalmic
Exam
6
Missing/
incomplete data
2,164
Complete
Data
Follow-up
2013/14
181 (41%) VI at baseline followed up
of which
24 (34%) Blind at baseline followed up
1,983 (53%)
Normal at
baseline and
followed-up
2,140 at risk
of going blind
29 New Blind
1,983 at risk
of going VI
234 New VI

Chapter 8. The incidence of diabetes mellitus and diabetic retinopathy in a population-based cohort study of people age 50 years and over in Nakuru, Kenya

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Student	Andrew Bastawrous
Principal Supervisor	Hannah Kuper
Thesis Title	The Nakuru Eye Disease Cohort Study

If the Research Paper has previously been published please complete Section B, if not please move to Section C

SECTION B – Paper already published

Where was the work published?	BMC Endocrine Disorders		
When was the work published?			
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Student Signature: A. Bastawrous **Date:** 12, April 2017

Supervisor Signature: H Kuper **Date:** 12, April 2017

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RESEARCH ARTICLE Open Access

The incidence of diabetes mellitus and diabetic retinopathy in a population-based cohort study of people age 50 years and over in Nakuru, Kenya

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Abstract

Background: The epidemic rise of diabetes carries major negative public health and economic consequences particularly for low and middle-income countries. The highest predicted percentage growth in diabetes is in the sub-Saharan Africa (SSA) region where to date there has been no data on the incidence of diabetic retinopathy from population-based cohort studies and minimal data on incident diabetes. The primary aims of this study were to estimate the cumulative six-year incidence of Diabetes Mellitus (DM) and DR (Diabetic Retinopathy), respectively, among people aged ≥50 years in Kenya.

Methods: Random cluster sampling with probability proportionate to size were used to select a representative cross-sectional sample of adults aged ≥50 years in 2007-8 in Nakuru District, Kenya. A six-year follow-up was undertaken in 2013–14. On both occasions a comprehensive ophthalmic examination was performed including LogMAR visual acuity, digital retinal photography and independent grading of images. Data were collected on general health and risk factors. The primary outcomes were the incidence of diabetes mellitus and the incidence of diabetic retinopathy, which were calculated by dividing the number of events identified at 6-year follow-up by the number of people at risk at the beginning of follow-up. Age-adjusted risk ratios of the outcomes (DM and DR respectively) were estimated for each covariate using a Poisson regression model with robust error variance to allow for the clustered design and including inverse-probability weighting.

Results: At baseline, 4414 participants aged ≥50 years underwent complete examination. Of the 4104 non-diabetic participants, 2059 were followed-up at six-years (50 · 2%). The cumulative incidence of DM was estimated at 61 · 0 per 1000 (95% CI: 50 · 3–73 · 7) in people aged ≥50 years. The cumulative incidence of DR in the sample population was estimated at 15 · 8 per 1000 (95% CI: 9 · 5–26 · 3) among those without DM at baseline, and 224 · 7 per 1000 (116.9–388.2) among participants with known DM at baseline. A multivariable risk factor analysis demonstrated increasing age and higher body mass index to be associated with incident DM. DR incidence was strongly associated with increasing age, and with higher BMI, urban dwelling and higher socioeconomic status.

Conclusions: Diabetes Mellitus is a growing public health concern with a major complication of diabetic retinopathy. In a population of 1 · 6 million, of whom 150,000 are ≥50 years, we estimated that 1650 people aged ≥50 develop DM per year, and 450 develop DR. Strengthening of health systems is necessary to reduce incident diabetes and its complications in this and similar settings.

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Background

The number of adults with Diabetes Mellitus (DM) in Africa is predicted to double from 12 · 1 million in 2010 to 23 · 9 million in 2030 based on projections from prevalence data [1]. The epidemic rise of DM carries major public health and economic consequences for the continent, particularly given it is home to some of the fastest growing economies and most rapid transitions in lifestyles conducive to DM ([http://unstats.un.org/unsd/methods/m49/m49regin.htm - least]). Currently, there are few incidence data from low and middle-income settings, particularly sub-Saharan Africa (SSA), making it difficult to plan screening and treatment services [2, 3].

DM causes visual impairment through cataract and diabetic retinopathy (DR) [4], a progressive disease of the retinal microvasculature. DR is not yet a leading cause of blindness in sub-Saharan Africa, responsible for just 2.8% of blindness [5]. However, it is likely to become an increasingly important cause of blindness and visual impairment, with the increasing prevalence of DM in SSA, and improving control of other leading causes of visual impairment such as cataract, uncorrected refractive error and trachoma. Population-based incidence data for DR are lacking for SSA, although some clinical follow-up data are available [6].

Current strategies to control DM in SSA focus on health system strengthening to enable a public health approach to both prevent the onset of DM and create awareness of the consequences of DM, including sight loss [7]. In addition, efforts are also being scaled-up for the identification of people with DM , and their enrolment in treatment programmes [8]. Systematic DR screening in SSA is currently very limited, with only a small number of locations having an active programme [9].

Data on the incidence and progression of DM and DR are needed to estimate the current and future burden of these conditions in order to inform service development, and future research. The primary aims of this study were to estimate the cumulative six-year incidence of DM and DR in people aged ≥50 years in Kenya. A secondary aim was to identify risk factors for each of these outcomes.

Methods

The fieldwork was carried out in Nakuru district, Kenya, which has a population of 1.6 million [accurate as of 2009], one third of which is urban. Nakuru is broadly representative of Kenya in terms of ethnic diversity and economic activities. The baseline survey took place from January 2007 to November 2008, and the follow-up survey from November 2012 to March 2014. Full details of the methods at baseline and follow-up are presented elsewhere [10–12].

Sampling strategy and recruitment at baseline

We selected 100 clusters of 50 people aged ≥50 years through probability proportionate to size sampling, using the electoral roll as the sampling frame. Households were selected within clusters using a modified compact segment sampling method [13]. The village leaders produced a sketch map of the polling area. The polling area was divided into segments each including approximately 50 people aged ≥50 years. One segment was chosen at random by drawing lots and all households in the segment were included in the sample sequentially, until 50 people aged ≥50 years were identified. If the segment did not include 50 people aged ≥50 years then an additional segment was chosen at random and sampling continued.

The enumeration team visited households, assisted by a village guide, and invited all eligible participants aged ≥50 years to the examination clinic, held at a convenient place in the cluster over the subsequent two days. Eligible participants were defined as those aged ≥50 years resident in the cluster (i.e. living there at least 6 months per year) who had slept in the house either the night before or were planning on sleeping in the house that night. If an eligible person was absent then the survey team revisited the household at least twice.

The six-year follow-up assessment was initiated by an Advance Team who visited homes of baseline participants and confirmed their identity using National Identity cards. The two advance teams comprised of one nurse, one field officer and a driver or public transport. During this visit they located individuals with assistance from the guide, phone numbers when available and previously recorded GPS locations using a Garmin Oregon 450 Satellite Navigation device. In addition, the team explained details of the examination and obtained written/thumb print informed consent as well as informing participants about location and time of examination [11].

Data collection

Comprehensive data were collected at baseline and follow-up, using comparable methods, including slit lamp examination by an ophthalmologist at both time points. Details of data collection are available elsewhere [11, 14] with specific details provided here for the current analyses.

Diabetes mellitus

A single random finger-prick blood sample was taken to measure glucose (Accutrend GC system) at baseline and at follow-up. At follow-up, in addition, subjects with a random blood sugar greater than 11.1 mmol/L (International Diabetes Federation (IDF) guidance at time of baseline study), those with known DM (regardless of random measure), evidence of DR on retinal imaging

and a subset (chosen randomly within each cluster) with random glucose between 7 and 11 mmol/L had an additional capillary blood HbA1C (A1C Now+, Bayer).

Visual acuity (VA)

Two ophthalmic nurses measured presenting VA, which was defined as the number of letters read correctly without glasses if the participant did not have glasses or with distance glasses if they had them. Each eye was tested separately at 4 m using a reduced Logarithm of the Minimal Angle of Resolution (LogMAR) tumbling 'E' chart [15] in a well illuminated area. If the subject's vision was too poor to read any letters on the chart at four meters, then the subject was tested at one meter, then counting fingers, hand movements, light perception or no light perception.

Fundus photography

Pupil dilation was performed using one drop of tropicamide 1% and one drop of phenylephrine 2.5%. The participants had two non-stereoscopic digital 45^0 fundus photographs taken per eye by an ophthalmic clinical officer using a TRC-NW6S Non-Mydriatic Retinal Camera with 10 megapixel Nikon D80 (TopCon®) at baseline and a Haag-Streit DRS CentreVue + at follow-up. One image was centred on the optic disc while the other was centred on the macula.

Anthropometric data collection

At baseline and follow-up, a nurse recorded the blood pressure of participants three times on the right arm of the participant, at least five minutes apart after an initial period of five minutes of rest using the Omron digital automatic monitor (model HEM907). Weight was measured to the nearest kilogram using standard scales (Seca 761 scales) after the participant had removed all heavy clothing and shoes. Height was measured to the nearest centimetre while the participant stood without shoes using a standardized stadiometer (Leicester Height Measure). For weight and height the average of two readings was recorded. Waist and hip circumferences were measured with a tape to the nearest centimetre.

Interviews

Participants were interviewed by trained nurses. Information was collected on demographic data, education and asset ownership. People were asked whether their mother tongue was "Kikuyu", "Kalenjin" (the two largest ethnic group in Nakuru County) or "other" to assign ethnicity. Information was also collected on health behaviour (smoking, alcohol use) and health status (diagnosis of diabetes or hypertension, family history and their treatment).

Grading of retinal images

Retinal images were forwarded to the Retinal Grading Centre at Moorfields Eye Hospital Reading Centre (MEHRC) London for grading DR. All images supplied by the Nakuru Eye Study Group, regardless of quality, were sent for grading. No manipulation of the images was allowed while grading, other than using grey-scale for viewing the images. All images were first categorized for quality as excellent, good, borderline and ungradeable.

Next, the photographs were graded for DR based on the UK National Guidelines on Screening for Diabetic Retinopathy [16]. Each eye was classified for all people with diabetes as: no DR, mild NPDR, moderate NPDR, severe NPDR or proliferative DR, based on the following criteria:

- No DR - no changes characteristic of diabetic retinopathy visible on the images.
- Mild non-proliferative DR (NPDR) - micro aneurysms (MAs) and retinal haemorrhages only were seen.
- Moderate NPDR - in addition to MAs multiple deep, round or blot haemorrhages were noted.
- Severe NPDR - the presence of features of NPDR plus cotton wool spots. In this scenario the grader was asked to search for vascular features of DR, such as venous loop, venous beading and Intra-retinal micro-vascular abnormality (IRMA). If these were found, severe NPDR was graded.
- Proliferative DR (PDR) – as above, with new vessels on the disc (NVD) new vessels elsewhere (NVE), pre-retinal or vitreous haemorrhage or pre-retinal fibrosis ± tractional retinal detachment were seen.

All images were graded by the senior grader. In case of difficulties, the adjudicator (TP) adjudicated the images. The adjudicator also looked at a random selection of 5% of images to ensure quality control. Data were entered onto Excel and checked for consistency by a data monitor. Grading methods were the same at baseline and follow-up.

Data analysis

Definitions and statistical analyses

DM was defined as per WHO standards for population-based studies: reported current medication (tablets or insulin) or; diet control for diabetes or; random blood glucose level ≥11 · 1 mmol/L [17]. At follow up the definition included HbA1C when a result was possible. HbA1C of > =7 · 0 was taken as confirmation of DM and if <7 · 0 DM was excluded. An HbA1C result superseded other measures of DM apart from self-reported and on medication, in which case an HbA1C of <7 · 0 was taken as well controlled DM and HbA1C > =7 · 0 of poorly controlled DM.

A continuous socio-economic score (SES) was produced for each participant using principal component analysis based on asset ownership, household type and education [18]. The score was divided into quartiles to categorize the study participants into four socioeconomic groups with a higher score representing higher SES. Body Mass Index (BMI) was calculated as height (meters)/weight (kilograms)^2. The clusters were defined as *rural or urban* according to the classification used by the District Health Statistics office [19].

All participants who had complete examinations at baseline who did not have DM or did not have DR were considered "at-risk" for incident DM or DR, respectively. Follow-up status at 6 years was categorised as i) Found and examined; ii) Found and not examined; iii) Deceased; iv) Moved away; or v) Unknown.

Statistical analysis was performed using STATA v13 (Stata Corp). All analysis accounted for the cluster survey design using Taylor linearized variance estimation to calculate standard errors.

Pearson chi-squared tests, corrected for the survey-design were used to calculate p-values in order to assess differences between participants seen and those lost to follow-up (LTFU), and between those known to have died and with unknown outcome status. Those who were deceased were then excluded. Those followed up but without complete records for all covariates at baseline were also excluded. An inverse probability-weighting (IPW) model [20] was developed to allow estimation of cumulative incidence while accounting for those LTFU. Multivariable logistic regression was used to identify independent baseline covariates associated with LTFU. Covariates for which there was evidence of univariable association with being LTFU ($p < 0.1$) were kept in a multivariable model. From this final model, the probability of being followed-up was estimated, based on the presence or absence of each of these baseline covariates. The inverse of this probability formed the weighting to be applied in order to account for those LTFU. The final step was to remove those individuals LTFU from the cohort, so that all subsequent analysis would be performed on only those with complete outcome records, with IPW applied to account for those LTFU. A sensitivity analyses for this approach involved a complete records analysis (i.e. only including those people who had complete records for outcome and all variables in the analysis).

The six-year cumulative incidence of each outcome was calculated by dividing the number of events identified at 6-year follow-up by the number of people at risk at the beginning of follow-up. 95% confidence intervals were estimated assuming a Poisson distribution of events. This analysis was done for the population overall, and stratified by key covariates. Age-adjusted risk ratios of the outcomes (DM and DR respectively) were estimated for each covariate using a Poisson regression model with robust error variance to allow for the clustered design and including IPW. For multivariable analysis, an initial model was fitted that included those variables associated with outcome in age-adjusted analysis (Wald p-value <0.05). A backward stepwise approach was applied to obtain a final multivariable model, removing variables with $p > 0.05$. Estimates were weighted to allow for any bias due to loss to follow up by weighting using inverse probability weights as described above. The six-year cumulative incidence was then used to estimate the expected number of new DR cases per year by multiplying the six-year incidence by the estimated Kenyan population and dividing by six, with the assumption that cumulative incidence was constant over time. Annual cumulative incidence was also estimated separately for men and women and in ten-year age categories (50–59, 60–69, 70–79 and 80 + .

Results

Diabetes mellitus

At baseline, 4414 participants aged ≥50 years underwent complete examination (response rate of 88 · 1%) and 4388 (99 · 4%) had DM status data available, of whom 287 (6 · 5%) were diagnosed with DM (Fig. 1). Of the 4,101who had no DM at baseline, 2059 (50 · 2%) were followed-up at six-years. Complete DM status data at follow-up were available on 2056 (99 · 9%) participants, of whom 123 (6 · 0%) were newly diagnosed with DM at six-year follow-up (Fig. 1).

Baseline characteristics of individuals with known baseline DM status data who were re-examined at follow-up (participants) and those who were LTFU are shown in Table 1. There was strong evidence that those who were LTFU were less likely to be Kikuyu or Kalenjin speakers and more likely to be from urban areas ($p <$ 0.001). The mean follow-up time of all participants was 5 · 6 (SD 0 · 6) years and the median was 5 · 5 (interquartile range (IQR): 5 · 0–6 · 1) years (referred to as "six-year cumulative incidence" from here on).

Of the 123 participants who developed incident DM by six-years, 64 diagnoses were self-reported and 59 were based on blood sugar readings. Of the 64 self-reported subjects with DM, 35 (54 · 7%) had random and HbA1C readings within normal limits and were considered "controlled DM", and the remaining 29 were "uncontrolled DM" (10 had high HbA1C only, three had elevated random glucose data only (no HbA1C data) and 16 had both a high random glucose and HbA1C). Consequently, the cumulative incidence of DM was estimated at 61 · 0 per 1000 (95% CI: 50 · 3,73 · 7) in people aged ≥50 years when corrected for loss to follow-up. The incidence of DM decreased with age in both men and women, and was similar across the sexes (Table 2). Based on recent census data, the number of incident

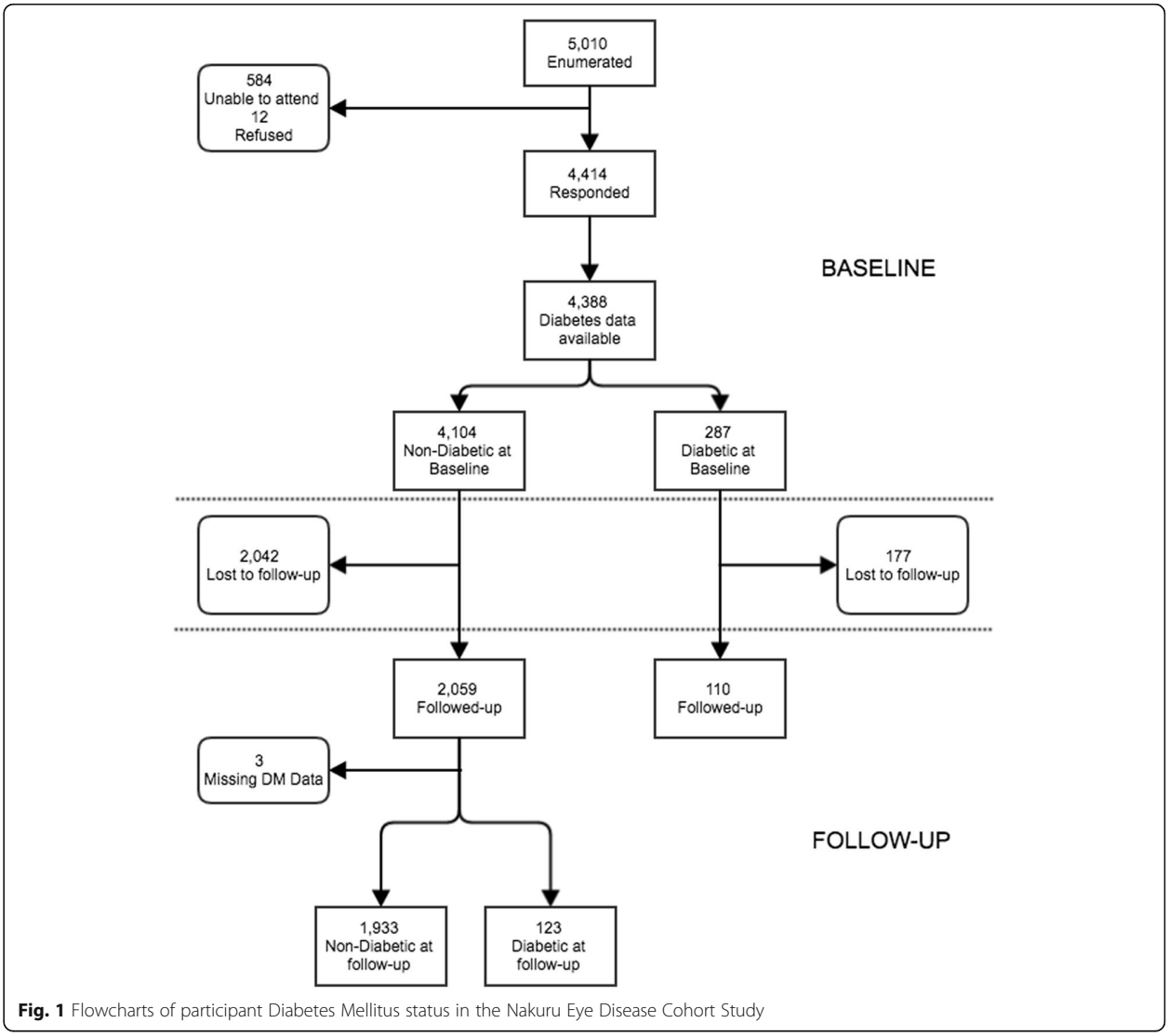

Fig. 1 Flowcharts of participant Diabetes Mellitus status in the Nakuru Eye Disease Cohort Study

cases was estimated by extrapolating to the Kenyan population aged ≥50 years (Table 3), assuming an equal incidence per year over the study period. In the population of 1·6 million people in Nakuru, Kenya, approximately 150,000 individuals are aged ≥50 years, and of these approximately 1650 will develop DM each.

Of the 287 participants with known DM from baseline, 54 (18.8%) were known to have died, 110 (38.3%) were re-assessed and 123 (42.8%) were LTFU. All 110 people with known DM at baseline were defined as having known DM at follow-up regardless of self-report. Of these, 70 (63·6%) self-reported as DM at follow-up, of whom 20 (28·6%) were controlled. Of the 40 with known DM at baseline who did not report as having DM at follow-up, 32 (80·0%) were controlled. Of these, 25 had a normal random blood sugar at baseline but self-reported as DM, four did not self-report but had a high random blood sugar and three both self-reported and had a high blood sugar.

Increased risk of incident DM was associated with the following baseline variables: higher body mass index, urban dwelling, higher socioeconomic status, hypertension, and having no previous formal education (Table 4). A lower incidence was found with increasing age, former alcohol consumption and Kalenjin ethnicity. After adjustment for confounding, increasing age and higher body mass index remained associated with incident DM (Table 4).

Diabetic retinopathy

At baseline, 4414 participants aged ≥50 years underwent complete examination (response rate of 88·1%) and 3281 (74·3%) had DR image data available, of whom 195 (5·9%) were diagnosed with DM at baseline (Fig. 2). Of these 195 participants, 70 had DR at baseline. At

Table 1 Baseline characteristics of all individuals with a known baseline DM status subdivided by their follow-up category (participant, non-participant) at 6-year follow-up ($N = 4388$)

Baseline characteristics		Missing values	Participants	Non-participants or not included in analysis			
			Followed-up $n = 2166$ (49.4%)	Not followed-up Alive/Unknown/DM status missing $n = 1814$ (41.3%)	*p*-value*	Deceased $n = 408$ (9.3%)	*p*-value**
Age in years, mean (SD)		0	62.7 (9.4)	62.6 (10.4)	0.84	71.6 (12.8)	<0.001
Systolic BP in mmHg, mean (SD)		12	139.5 (23.5)	140.8 (24.8)	0.16	147.4 (30.3)	<0.001
Diastolic BP in mmHg , mean (SD)		12	82.6 (13.0)	83.3 (13.6)	0.19	82.7 (16.5)	0.94
Random Blood Glucose, mean (SD)		92	5.1 (2.3)	5.3 (2.3)	0.12	5.7 (3.7)	<0.001
Sex, % (n)	Female	0	1025 (47.3%)	841 (46.4%)	0.59	236 (57.8%)	<0.001
	Male		1141 (52.7%)	973 (53.6%)		172 (42.2%)	
BMI, % (n)	Underweight (<18.5 kg/m^2)	42	267 (12.4%)	250 (14.0%)	0.52	99 (25.0%)	<0.001
	Normal (18.5–24.99 kg/m^2)		1091 (50.5%)	882 (49.2%)		199 (50.3%)	
	Overweight (25–29.99 kg/m^2)		506 (23.4%)	419 (23.4%)		66 (16.7%)	
	Obese (30 + kg/m^2)		295 (13.7%)	240 (13.4%)		32 (8.1%)	
Vision status impaired (<6/12 better eye), % (n)	Normal	17	1985 (91.7%)	1635 (90.8%)	0.36	306 (75.4%)	<0.001
	Impaired		180 (8.3%)	165 (9.2%)		100 (24.6%)	
Tribe, % (n)	Kikuyu	0	1393 (64.3%)	1079 (59.5%)	<0.001	283 (69.4%)	0.09
	Kalenjin		540 (24.9%)	380 (20.9%)		92 (22.5%)	
	Other		233 (10.8%)	355 (19.6%)		33 (8.1%)	
Education, % (n)	None	1	193 (8.9%)	204 (11.3%)	0.03	26 (6.4%)	<0.001
	Primary		687 (31.7%)	588 (32.4%)		179 (43.9%)	
	Secondary		1069 (49.4%)	806 (44.5%)		174 (42.6%)	
	Higher		217 (10.0%)	215 (11.9%)		29 (7.1%)	
Residence, % (n)	Rural	0	1636 (75.5%)	1014 (55.9%)	<0.001	302 (74.0%)	0.59
	Urban		530 (24.5%)	800 (44.1%)		106 (26.0%)	
SES Quartile, % (n)	Lower	22	514 (23.8%)	442 (24.5%)	0.01	136 (33.3%)	0.003
	Middle lower		591 (27.4%)	404 (22.4%)		96 (23.5%)	
	Middle upper		557 (25.8%)	438 (24.3%)		97 (23.8%)	
	Upper		495 (22.9%)	517 (28.7%)		79 (19.4%)	
Smokers, % (n)	Never	0	1503 (69.4%)	1322 (72.9%)	0.007	255 (62.5%)	0.02
	Former		163 (7.5%)	145 (8.0%)		33 (8.1%)	
	Current		500 (23.1%)	347 (19.1%)		120 (29.4%)	
Alcohol, % (n)	Never	5	882 (40.8%)	704 (38.9%)	0.10	117 (28.7%)	<0.001
	Former		942 (43.6%)	772 (42.6%)		221 (54.2%)	
	Current		339 (15.7%)	336 (18.5%)		70 (17.2%)	

*P-value for association between the baseline characteristic and the odds of having a known DM status observation at follow up, amongst all participants identified as non-diabetic at baseline and not known to be deceased at follow up

**P-value for association between the baseline characteristic and the odds of dying during the follow up period, amongst all participants identified as non-diabetic at baseline and either followed up or known to be deceased at follow up (i.e. excluding the group who were not followed up)

follow-up, 78 (40 · 0%) of the 195 participants with baseline DM were seen, and 1562 (50 · 6%) of the 3086 participants without DM at baseline.

The baseline characteristics of those with complete data for analysis (participants with a known DR status at follow-up, based on retinal images), and those for whom data was incomplete were similar. However a higher proportion of those who had impaired vision at baseline were not included in the DR incidence analysis, either due to LTFU or ungradeable retinal images (Table 5).

Table 2 Age-gender–specific 6-year cumulative incidence of diabetes mellitus among the Nakuru eye disease cohort study participants

	Male		Female		Overall	
Age group (years)	N (Cases / at risk)	Risk per 1000/6 years (95% CI)[a]	N	Risk per 1000/6 years (95% CI)[a]	N	Risk per 1000/6 years (95% CI)[a]
Diabetes Mellitus (*N* = 2056)						
50–59	24 / 393	63.7(43.0,93.3)	37 / 544	69.6(49.2,97.7)	61 / 937	67.1(52.2,85.8)
60–69	19 / 328	62.3(39.2,97.6)	22 / 326	67.0(42.6103.8)	41 / 654	64.7(46.3,89.5)
70–79	8 / 180	48.2(22.2101.5)	9 / 151	57.5(29.9107.8)	17 / 331	52.6(33.0,82.7)
80+	3 / 66	40.3(12.3123.9)	1 / 68	11.9(1.6,84.9)	4 / 134	25.8(9.6,67.5)
All ages	54 / 967	58.6(44.7,76.4)	69 / 1089	63.0(48.8,81.1)	123 / 2056	61.0(50.3,73.7)
Diabetic Retinopathy – among those without DM and without DR at baseline (*N* = 1421)						
50–59	5 / 297	24.6(8.5,68.9)	7 / 394	20.0(7.8,50.3)	12 / 691	22.0(11.0,43.4)
60–69	5 / 237	22.9(9.8,53.0)	1 / 229	3.9(0.5,28.5)	6 / 466	13.3(5.4,32.8)
70–79	2 / 123	15.2(3.6,61.4)	0 / 89	–	2 / 212	8.6(2.1,34.8)
80 + [b]	0 / 29	–	0 / 23	–	0 / 52	–
All ages	12 / 686	20.5(10.9,38.2)	8 / 735	11.5(4.8,27.1)	20 / 1421	15.8(9.5,26.2)
Diabetic Retinopathy – among those with DM at baseline, but without DR at baseline (*N* = 44)						
50–59	3 / 8	400.4(83.3830.7)	3 / 14	198.9(46.8556.8)	6 / 22	278.3(111.7541.7)
60–69	4 / 10	409.8(130.2763.1)	0 / 4	–	4 / 14	268.8(78.8612.2)
70–79	1 / 4	175.5(2.7943.6)	0 / 2	–	1 / 6	126.8(6.3770.0)
80 + [b]	0 / 1	–	0 / 1	–	0 / 2	–
All ages	8 / 23	337.7(162.1573.3)	3 / 21	118.8(29.7372.5)	11 / 44	224.7(116.9388.2)

[a]Estimated using inverse probability weights to account for loss to follow up
[b]No-one with DR at follow up among 80+ group
Risk of the outcome in the 6-year follow up, adjusted for loss to follow up using inverse probability weightings
Sample sizes are small for the DR analyses, so estimates have a wide confidence interval

Of the 1562 people without either DM or DR at baseline, 1377 (88 · 1%) had complete follow-up DR status data. Of these, 89/1377 (6 · 5%) were newly diagnosed with DM; and 9 (10 · 1%) had incident DR. A further 11 incident cases of DR were seen in the 44 participants with DM but no DR at baseline (Fig. 2). Therefore, in total, 20 participants developed DR during follow up, giving a corrected cumulative incidence of 15 · 8 per 1000 (95% CI: 9 · 5–26 · 3), Table 2. This equates 15,800 cases in the population aged ≥50 years per year per million. In the population of 1 · 6 million people in Nakuru, Kenya, approximately 150,000 individuals are aged ≥50 years, and of these approximately 1650 will develop DM each year and 450 will develop DR each year.

Among subjects with known DM at baseline, the corrected cumulative incidence of DR is 224 · 7 per 1000 (95% CI: 116 · 9–388 · 2) (Table 2). Similarly to DM, the incidence of DR decreased with increasing age (Table 2). Of the 20 incident cases of DR, seven had sight-threatening DR (STDR) of whom two cases were proliferative DR (five with severe retinopathy), four cases had moderate DR and nine mild DR (Table 2).

In total 23 participants with known DR at baseline were followed up and had a gradable retinal image. Of these, 15 still had signs of DR, while eight no longer had evidence of DR. Of nine with background DR at baseline, one progressed to pre-proliferative DR and the remainder either remained BDR ($n = 2$) or had no signs of DR at follow-up ($n = 6$). Of seven participants with moderate non-proliferative DR (NPDR) at baseline, three progressed to proliferative DR (PDR). One participant with severe NPDR at baseline developed PDR and one remained Severe NPDR. Of five with PDR at baseline, one regressed to Moderate NPDR (having undergone pan-retinal photocoagulation) and the other four remained PDR, of whom two had evidence of laser treatment.

Multivariable analysis of incident DR (Table 6) was not conducted due to the small number of participants in the category ($n = 20$). However, the age-adjusted risk ratio suggested a correlation between increasing incidence of DR and higher BMI, urban dwelling and higher socioeconomic status. No conclusions can be drawn from this due to the wide 95% confidence intervals.

Discussion

This population-based cohort study of people aged 50+ in rural Kenya is the first, to our knowledge, to assess the incidence of DM and DR in SSA. The six-year

Table 3 Extrapolated number of new adults, per year, aged 50 years and over in Kenya with diabetes mellitus and diabetic retinopathy based on incidence data (adjusted to take account of loss to follow up) and estimates of the population in Kenya by age group in 2015

	Male			Female			Overall		
Age group (years)	Extrapolated number	Lower (95% CI)	Upper (95% CI)	Extrapolated number	Lower (95% CI)	Upper (95% CI)	Extrapolated number	Lower (95% CI)	Upper (95% CI)
Diabetes Mellitus									
50–59	10,710	7230	15,690	12,760	9020	17,910	23,570	18,340	30,140
60–69	5350	3370	8390	7400	4700	11,460	12,690	9080	17,560
70–79	1950	900	4100	3010	1570	5650	4880	3060	7680
80+	490	150	1500	200	30	1430	750	280	1950
All ages	17,910	13,660	23,350	22,860	17,710	29,390	40,780	33,630	49,270
Diabetic Retinopathy – among those without DM and those without DR									
50–59	4230	1460	11,860	3850	1500	9690	8020	4020	15,840
60–69	2090	890	4820	450	60	3300	2760	1110	6770
70–79	640	150	2610	–	–	–	840	200	3410
80+	–	–	–	–	–	–	–	–	–
All ages	6520	3460	12,160	4390	1850	10,340	11,100	6670	18,370
Diabetic Retinopathy – among those without DR at baseline									
50–59	1650	340	3430	1850	430	5170	3790	1520	7390
60–69	2090	660	3880	–	–	–	2840	830	6470
70–79	370	10	1980	–	–	–	620	30	3780
80+	–	–	–	–	–	–	–	–	–
All ages	4300	2070	7310	2260	570	7100	7080	3690	12,240

All are based on 2015 estimates of population

Diabetes Mellitus: Population at risk are all adults over 50 who do not have DM. To estimate the size of the population at risk the 2008 DM prevalence is used. Expected number of new DM diagnoses in 50+ year old individuals per year is (population at risk x risk per 1000/6 years)/(6 × 1000)

Diabetic Retinopathy among those with no DM and without DR at baseline: Population at risk are all adults over 50 who do not have DR. To estimate the size of the population at risk the 2008 DR prevalence is used. Expected number of new DR diagnoses in 50+ year old individuals per year is (population at risk x risk per 1000/6 years)/(6 × 1000)

Diabetes Retinopathy among those with DM out without DR at baseline: Population at risk are all adults over 50 who have DM but do not have DR. To estimate the size of the population at risk the 2008 DR prevalence is used. Expected number of new DR diagnoses in those 50+ year old with DM per year is (population at risk x risk per 1000/6 years)/(6 × 1000)

Sample sizes are small for the DR analyses, so estimates have wide confidence intervals

cumulative incidence of DM in this study was 61 cases per 1000, equating to approximately 10 new cases per 1000 of population aged ≥50 per year. Longo-Mbenza et al. investigated the incidence of type 2 DM in a prospective cohort of 807 subjects of Central Africans aged ≥40 years over a four-year period, all of whom had no DM at basline [2]. During the follow up, there were 93 incident DM cases (11 · 5%), corresponding to an incidence of 29 (95% CI 15-43) per 1000 persons per year, considerably higher than our estimated cumulative incidence. Motola et al. investigated the incidence of DM in a prospective cohort of 563 South African Indians with no-DM aged 15 years or greater over a ten-year period. During the follow up period there were 91 (16.2%) incident cases of DM, corresponding to an incidence (age and sex-adjusted) cumulative incidence of 8.3 per 1000 persons per year [21]. This latter estimate was more in line with ours, but included a much younger population.

The six-year cumulative incidence of DR among persons, 50 years and over, with known DM was 225 cases per 1000 (95%CI: 116 · 9388 · 2). There is minimal comparable data available for SSA. One systematic review of 62 studies that reported the prevalence or incidence of DR in SSA [6] found few high-quality population-based studies and the majority were hospital or clinic based surveys. Two cohort studies of DR have been conducted in SSA. Sixty-four patients with insulin-dependent (Type 1) DM (IDDM) in Soweto, South Africa were followed over a 10-year period between 1982 and 1992. In those subjects seen at 10 years, prevalence of DR had increased from 6 to 52% and PDR from 0 to 3%, but no incidence data was reported [22]. In a two-year prospective cohort study of DR in Malawi, 357 subjects were systematically sampled from two primary care diabetes clinics, and 295 participants were followed up. The incidence of any DR over the follow-up period was 380

Table 4 Age-adjusted and multivariable analysis of a number of baseline co-variables and incident diabetes mellitus in the Nakuru eye disease cohort study

	Study sample, $n = 2056$				
	No at risk of diabetes mellitus	Incident diabetes mellitus	Risk per 1000/6 years (95% CI)	Age adjusted risk ratio (95% CI)	Multivariable adjusted risk ratio (95% CI)[a]
Age					
50–59	937	61	67.1 (52.2–85.8)	Baseline	Baseline
60–69	654	41	64.7 (46.3–89.5)	0.96 (0.64–1.45)	1.10 (0.74–1.63)
70–79	331	17	52.6 (33.0–82.7)	0.78 (0.47–1.30)	1.05 (0.64–1.72)
80+	134	4	25.8 (9.6–67.5)	0.38 (0.14–1.05)	0.58 (0.21–1.59)
Gender					
Male	967	54	58.6 (44.7–76.4)	Baseline	–
Female	1089	69	63.0 (48.8–81.0)	1.06 (0.74–1.51)	–
BMI (5 missing values)					
Underweight	260	5	17.5 (6.1–49.2)	Baseline	Baseline
Normal	1050	29	27.4 (18.5–40.4)	1.54 (0.50–4.79)	1.54 (0.50–4.79)
Overweight	465	54	120.4 (91.6–156.8)	6.69 (2.26–19.81)	6.69 (2.26–19.81)
Obese	276	34	123.3 (85.9–173.8)	6.83 (2.28–20.49)	6.83 (2.28–20.49)
Location					
Rural	1571	79	48.6 (39.2–60.1)	Baseline	–
Urban	485	44	87.0 (63.5–118.2)	1.75 (1.20–2.56)	–
SES Quartile (9 missing values)					
Lower	504	15	28.9 (17.9–46.5)	Baseline	–
Lower middle	576	26	46.8 (31.4–69.3)	1.59 (0.87–2.89)	–
Upper middle	520	40	75.4 (54.7–103.2)	2.54 (1.47–4.36)	–
Upper	447	41	94.3 (71.7–123.1)	3.12 (1.80–5.40)	–
Smoker					
Never	1426	88	62.6 (49.9–78.2)	Baseline	–
Former	161	4	31.4 (9.4–100.2)	0.50 (0.15–1.63)	–
Current	469	31	66.8 (47.8–92.7)	1.08 (0.73–1.62)	–
Hypertension (7 missing values)					
No	1084	44	43.3 (31.6–59.2)	Baseline	–
Yes	965	78	80.3 (64.1–100.3)	1.94 (1.33–2.82)	–
Alcohol (3 missing values)					
Never	835	60	73.0 (55.6–95.2)	Baseline	–
Former	891	42	47.5 (35.3–63.7)	0.68 (0.46–1.00)	–
Current	327	20	66.7 (41.8–104.9)	0.94 (0.55–1.61)	–
Ethnic group					
Kikuyu	1308	86	68.2 (53.5–86.6)	Baseline	–
Kalenjin	530	23	42.6 (28.3–63.6)	0.62 (0.40–0.98)	–
Other	218	14	60.5 (35.6–101.1)	0.84 (0.45–1.54)	–
Education level					
No education	173	14	88.9 (56.1–13.8)	1.77(1.01–3.12)	–
Primary	665	32	45.7 (31.8–65.4)	Baseline	–
Secondary	1009	61	61.6 (46.9–80.5)	1.25 (0.80–1.95)	–
College/Uni	209	16	80.0 (48.4–129.4)	1.58 (0.85–2.95)	–

[a]For multivariable analysis, an initial model was fitted that included those variables shown to be associated with outcome in age-adjusted analysis (using a Wald test threshold p-value of <0.05 to indicate association). A backward stepwise approach was then applied in order to obtain a final multivariable model, removing variables with $p > 0.05$ one-by-one

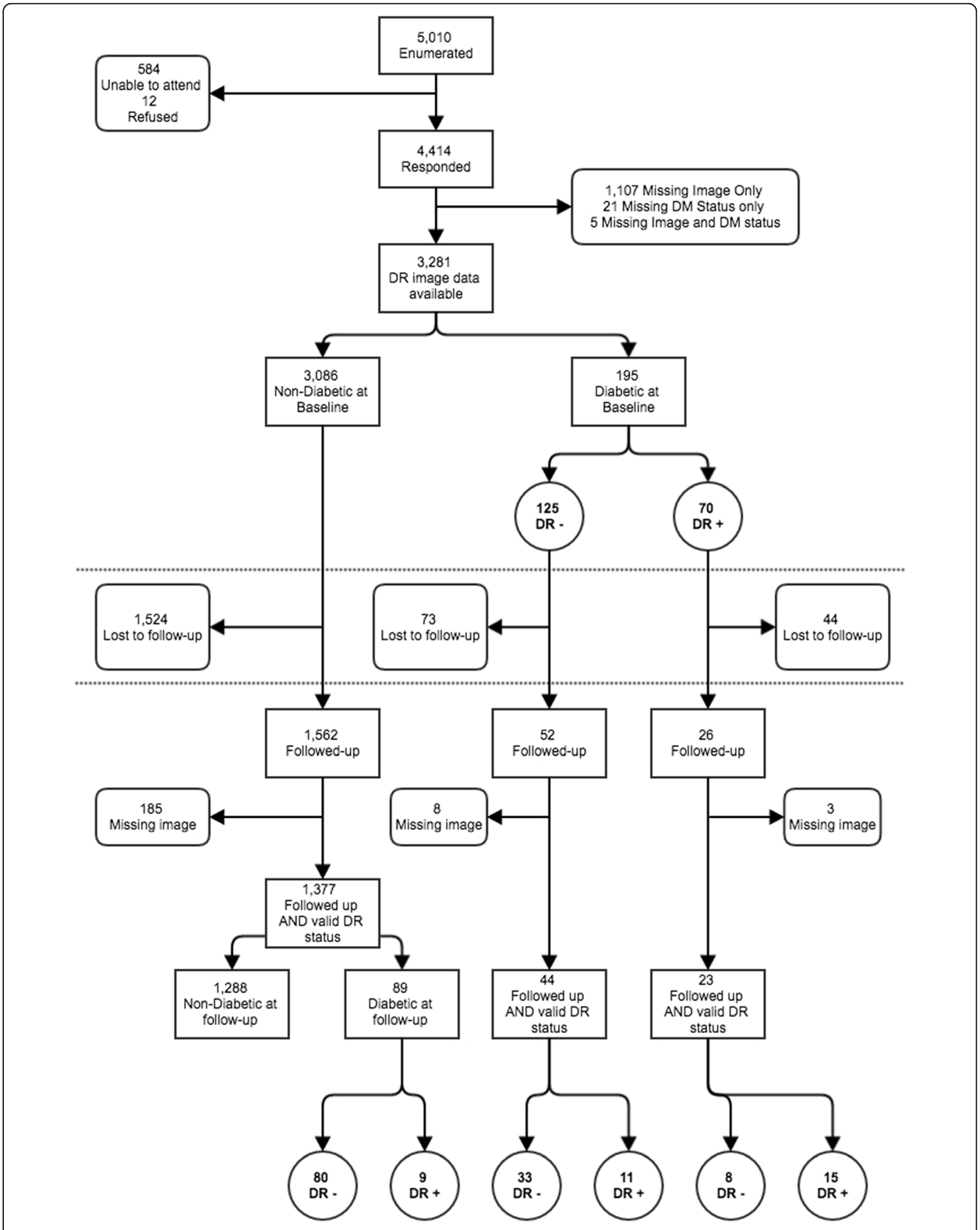

Fig. 2 Flowcharts of participant Diabetic Retinopathy status in the Nakuru Eye Disease Cohort Study. DM: Diabetes Mellitus, DR: Diabetic Retinopathy

Table 5 Baseline characteristics of all individuals with a known baseline DR status, subdivided by their follow-up category (participant, non-participant) at 6-year follow-up ($N = 3281$)

Baseline characteristics		Missing values	Participants	Non-participants or not included in analysis			
			Followed-up $n = 1444$ (44.0%)	Not followed-up Alive/Unknown/DM status missing $n = 1555$ (47.4%)	p-value*	Deceased $n = 282$ (8.6%)	p-value**
Age in years, mean (SD)		0	61.4 (8.6)	62.7 (10.2)	0.015	69.6 (11.8)	<0.001
Systolic BP in mmHg, mean (SD)		8	138.6 (23.6)	140.4 (24.1)	0.084	145.2 (29.6)	0.001
Diastolic BP in mmHg , mean (SD)		8	82.9 (13.0)	82.9 (13.1)	0.865	82.6 (16.4)	0.72
Random Blood Glucose, mean (SD)		69	5.1 (2.3)	5.2 (2.3)	0.10	5.5 (3.0)	0.04
Sex, % (n)	Female	0	701 (48.5%)	746 (48.0%)	0.78	172 (61.0%)	<0.001
	Male		743 (51.5%)	809 (52.0%)		110 (39.0%)	
BMI, % (n)	Underweight (<18.5 kg/m^2)	11	166 (11.5%)	220 (14.2%)	0.07	68 (24.2%)	<0.001
	Normal (18.5-24.99 kg/m^2)		738 (51.2%)	757 (48.9%)		138 (49.1%)	
	Overweight (25-29.99 kg/m^2)		343 (23.8%)	360 (23.3%)		51 (18.1%)	
	Obese (30 + kg/m^2)		194 (13.5%)	211 (13.6%)		24 (8.5%)	
Vision status impaired (<6/12 better eye), % (n)	Normal	4	1375 (95.3%)	1415 (91.1%)	<0.001	233 (82.9%)	<0.001
	Impaired		68 (4.7%)	138 (8.9%)		48 (17.1%)	
Tribe, % (n)	Kikuyu	0	912 (63.2%)	891 (57.3%)	0.001	191 (67.7%)	0.28
	Kalenjin		358 (24.8%)	354 (22.8%)		63 (22.3%)	
	Other		174 (12.0%)	310 (19.9%)		28 (9.9%)	
Education, % (n)	None	1	129 (8.9%)	168 (10.8%)	0.004	20 (7.1%)	0.001
	Primary		425 (29.4%)	518 (33.3%)		116 (41.1%)	
	Secondary		739 (51.2%)	685 (44.1%)		121 (42.9%)	
	Higher		151 (10.5%)	183 (11.8%)		25 (8.9%)	
Residence, % (n)	Rural	0	1062 (73.5%)	863 (55.5%)	<0.001	199 (70.6%)	0.43
	Urban		382 (26.5%)	692 (44.5%)		83 (29.4%)	
SES Quartile, % (n)	Lower	16	310 (21.6%)	385 (24.9%)	0.003	87 (30.9%)	0.03
	Middle lower		399 (27.7%)	354 (22.9%)		63 (22.3%)	
	Middle upper		386 (26.8%)	380 (24.6%)		72 (25.5%)	
	Upper		343 (23.9%)	426 (27.6%)		60 (21.3%)	
Smokers, % (n)	Never	0	981 (67.9%)	1115 (71.7%)	0.02	167 (59.2%)	0.02
	Former		113 (7.8%)	139 (8.9%)		23 (8.2%)	
	Current		350 (24.2%)	301 (19.4%)		92 (32.6%)	
Alcohol, % (n)	Never	3	586 (40.6%)	584 (37.6%)	0.06	82 (29.1%)	0.001
	Former		624 (43.2%)	664 (42.8%)		147 (52.1%)	
	Current		233 (16.1%)	305 (19.6%)		53 (18.8%)	

*P-value for association between the baseline characteristic and the odds of having a valid DM observation at follow up, amongst all participants identified as having no diabetes at baseline and not known to be deceased at follow up

**P-value for association between the baseline characteristic and the odds of dying during the follow up period, amongst all participants identified as no-DM at baseline and either followed up or known to be deceased at follow up (i.e. excluding the group who were not followed up)

per 1000 of population over two years [23]. Two of the leading cohort studies of eye disease from high-income settings, the Blue Mountains Study in Australia and The Wisconsin Epidemiologic Study of Diabetic Retinopathy (WESDR) in the United States in which comparable methodology was used show estimates of incident DR from Nakuru, Kenya are more than twice that of the findings from Wisconsin and three times that of the Blue Mountains Study. The Blue Mountains Study reported 222 cases per 1000 over five years (44 per

Table 6 Age-adjusted analysis the association between a number of baseline co-variables and incident DR amongst those DR free at baseline in the Nakuru eye disease cohort study

	Study sample, $n = 1421$			
	No at risk of diabetic retinopathy	Incident diabetic retinopathy	Risk per 1000/6 years (95% CI)	Age adjusted risk ratio (95% CI)
Age				
50–59	691	12	22.0 (11.0–43.4)	Baseline
60–69	466	6	13.3 (5.4–32.8)	0.6 (0.2–2.0)
70–79	212	2	8.6 (2.1–34.8)	0.4 (0.1–1.9)
80+	52	0	–	–
Gender				
Male	686	12	20.5 (10.9–38.2)	Baseline
Female	735	8	11.5 (4.8–27.1)	0.5 (0.2–1.5)
BMI (2 missing values)				
	166	1	5.3 (0.7–36.6)	Baseline
Underweight				
Normal	727	5	8.1 (3.3–19.5)	1.5 (0.2–13.0)
Overweight	336	11	39.6 (20.3–75.9)	6.4 (0.8–53.6)
Obese	190	3	12.9 (4.1–40.2)	2.0(0.2–21.9)
Location				
Rural	1053	12	11.6 (6.6–20.4)	Baseline
Urban	368	8	23.5 (10.3–52.7)	1.8 (0.7–4.4)
SES Quartile (6 missing values)				
Lower	309	1	3.0 (0.4–21.8)	Baseline
Lower middle	394	2	4.9 (1.2–19.4)	1.6 (0.4–6.9)
Upper middle	380	9	25.1(13.1–47.5)	7.5 (1.0–58.1)
Upper	332	8	29.3 (13.3–63.3)	8.3 (1.0–66.9)
Smoker				
Never	964	16	18.3 (10.0–33.1)	Baseline
Former	113	0	–	–
Current	344	4	14.3 (5.4–37.5)	0.8 (0.3–2.6)
Hypertension (2 missing values)				
No	764	8	15.0 (6.0–36.7)	Baseline
Yes	655	12	16.9 (9.3–30.3)	1.2 (0.4–3.6)
Alcohol (1 missing value)				
Never	580	8	15.3 (6.5–35.6)	Baseline
Former	611	9	15.0 (7.4–30.1)	1.1 (0.4–3.3)
Current	229	3	19.0 (4.1–83.5)	1.3 (0.2–7.9)
Ethnic group				
Kikuyu	895	14	16.9 (10.3–27.8)	Baseline
Kalenjin	357	3	8.5 (1.9–36.9)	0.5 (0.1–2.3)
Other	169	3	22.6 (7.2–69.1)	1.1 (0.4–3.0)
Education level				
No education	123	4	42.8 (15.3–114.2)	Baseline
Primary	422	0	–	–
Secondary	726	14	21.7(11.9–39.0)	0.6(0.2–1.9)
College/ Uni	150	2	12.6(3.0–51.6)	0.3(0.0–1.8)

For multivariable analysis, an initial model was fitted that included those variables shown to be associated with outcome in age-adjusted analysis (using a Wald test threshold p-value of <0.05 to indicate association). A backward stepwise approach was then applied in order to obtain a final multivariable model, removing variables with $p > 0.05$ one-by-one

1000/year) and the WESDR study reported 327 cases per 1000 over a four-year period (82 per 1000/year).

In a prospective cohort in southern Malawi, sampled from two primary care diabetes clinics, the 2-year incidence of sight-threatening DR (STDR) amongst 357 subjects for subjects with no DR, BDR, and PDR at baseline was 2 · 7% (95% confidence interval [CI], 0 · 1–5 · 3), 27 · 3% (95% CI, 16 · 4–38 · 2), and 25 · 0% (95% CI, 0–67 · 4), respectively [23].

The sample of participants with DR at both study time points in the Nakuru cohort was too small to draw conclusions on the progression of DR. However, 23 participants over the six year follow up period had a DR assessment at baseline and follow-up, of whom four progressed from non-STDR to STDR and of five with STDR at baseline, one recovered to non-STDR and the other four remained with STDR [23].

Strengths

This study is one of the first reports of DM and DR from a population-based sample in SSA. The sampling methodology ensures that the data is representative for the population over 50 and minimised bias by sampling from the community rather than from hospitals or clinics. Retinal image data were collected for DR analysis and images were independently graded at Moorfields Eye Hospital Reading Centre.

Limitations

The definition of DM used in this study was based on a single, non-fasting, capillary blood sample and did not include fasting blood glucose samples and HbA1C measures were only available at follow-up. There was a high loss to follow-up which creates potential for selection bias however statistical methods were used to adjust for this. This high LTFU was largely due to post-election violence in the region between the two study time points which led to mass displacement. The population under

Table 7 Population summary for programme planning based on prevalence and incidence data from a Kenyan cohort over 50 years of age

Population at risk		
Place	Nakuru County	Kenya (National)
Total Population	1.6 Million	46 Million
Population 50 years and over	0.15 Million	4.3 Million
Diabetes Mellitus (DM)		
Prevalence (%) of DM	6.5	
Number of people over 50 with DM (needing examination of the retina every 1–2 years)	26,100	279,500
Awareness of DM within the population over 50 (%)	85	
Number of people over 50 with known DM	22,185	237,575
Number over 50 who develop new DM per 1000 of population per year	11/1000	
Number over 50 who develop new DM per sample population per year	1650	47,300
Diabetic Retinopathy (DR)		
Proportion (%) of people over 50 with DM who have DR	35.9	
Number of people over 50 with DR	9400	100,340
Number over 50 who develop new DR per 1000 of population per year	3/1000	
Number over 50 who develop new DR of the sample population per year	450	12,900
Vision Threatening Diabetic Retinopathy (VTDR)		
Proportion of people over 50 with DM who have VTDR	13.4	
Number of people over 50 with VTDR (needing treatment)	1260	13,450
Number over 50 who develop new VTDR per 1000 of population per year	1.6/1000	
Number over 50 who develop new VTDR of the sample population per year	240	6880

Further research needs to be done to assess gaps in the patient care pathway which include:
- awareness of DM in the population;
- access / availability to relevant diagnostic and treatment services ;
- quality of diagnostic and treatment services;
- availability of screening for DR within diabetes and eye care;
- protocols and referral thresholds for people with or without DR;
- barriers to receiving treatment for STDR in those with known STDR

observation were ≥50 years and therefore the study does not estimate the incidence of DM or DR in the population under age 50 years.

Implications

As the diabetes epidemic continues, a greater understanding is required of the resources needed and level of deployment of those resources within the health system to respond appropriately. This includes primary prevention of DM in the community, high treatment coverage of persons with DM in primary care, and inclusion of eye screening for people with DM as standard practice. With good prevalence data on DM available in many countries and regions in SSA and a growing understanding of the natural history of the diseases in different populations it should now be possible (within a wide range of confidence and based on several assumptions) to estimate the conversion in the over 50s of those without DM developing DM and DR.

Overall, DM is increasing in Africa probably related to environmental factors such as increased access to processed foods and more sedentary lifestyles; this is likely to increase in the next decade. The awareness of DM in the community is still low [3] and public campaigns to raise awareness as well as provide locally available DM screening and counselling facilities is needed. It is also important to consider detection of VTDR in the community and resourcing eye care providers with the knowledge and tools to manage patients with STDR is essential to ensure a high quality service and avoid sight loss from DM. Specific planning data for the region under investigation is provided in Table 7.

Conclusions

In a population of 1·6 Million in Nakuru County, Kenya: 150,000 are 50 years and over, we estimated that 1650 people over the age of 50 develop DM per year, and 450 develop DR. The management of DM and DR is complex and requires different approaches at different levels of the healthcare system with considerable variation depending on location. For effective planning at any level, high quality information is required to effectively plan the services. This cohort provides some data to support planning and is indicative of areas that need further research.

Abbreviations

BDR: Background diabetic retinopathy; DM: Diabetes mellitus; DR: Diabetic retinopathy; LTFU: Lost to follow up; NPDR: Non-proliferative diabetic retinopathy; PDR: Proliferative diabetic retinopathy; SSA: Sub Saharan Africa; VI: Visual impairment; VTDR: Vision threatening diabetic retinopathy

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Availability of data and materials

The datasets used and/or analysed during the current study available from the corresponding author on reasonable request.

Authors' contributions

AB Study design, Data collection, Analysis, wrote manuscript, reviewed/edit manuscript. WM Study design, Data collection, Analysis, reviewed/edit manuscript. KW Analysis, reviewed/edit manuscript. MB Study design, Data

collection, Analysis, reviewed/edit manuscript. HR Data collection, reviewed/edit manuscript. HAW Study design, Analysis, reviewed/edit manuscript. DM Analysis, wrote manuscript, reviewed/edit manuscript. AF Study design, Analysis, reviewed/edit manuscript. TP Study design, Data collection, Analysis, reviewed/edit manuscript. PB Data collection, reviewed/edit manuscript. MB Study design, Data collection, Analysis, wrote manuscript, reviewed/edit manuscript. HK Study design, Data collection, Analysis, wrote manuscript, reviewed/edit manuscript. All authors read and approved the final manuscript.

Competing interests
The authors declare that they have no competing interests.

Consent for publication
N/A.

Ethics approval and consent to participate
The London School of Hygiene & Tropical Medicine (LSHTM) Ethics committee and the African Medical Research Foundation (AMREF) granted ethical approval for the study. Approval was also granted by the Provincial Medical Officer for Nakuru County. Written approval was sought from the administrative heads in each cluster, usually the village chief. All participants gave written or thumbprint consent to participate. People requiring medical treatments were referred to the appropriate centre.

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Chapter 9. Six-Year Incidence of Age-Related Macular Degeneration in Kenya

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Student	Andrew Bastawrous
Principal Supervisor	Hannah Kuper
Thesis Title	The Nakuru Eye Disease Cohort Study

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SECTION B – Paper already published

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JAMA Ophthalmology | Original Investigation

Six-Year Incidence and Progression of Age-Related Macular Degeneration in Kenya
Nakuru Eye Disease Cohort Study

Andrew Bastawrous, BSc (Hons), MRCOphth; Wanjiku Mathenge, PhD; Tunde Peto, PhD; Nisha Shah, MSc; Kevin Wing, PhD; Hillary Rono, MMed, MPHEC; Helen A. Weiss, MSc, DPhil; David Macleod, MSc; Allen Foster, FRCS; Matthew Burton, PhD, FRCOphth; Hannah Kuper, ScD

IMPORTANCE The incidence of age-related macular degeneration (AMD) is unknown in Africa.

OBJECTIVE To estimate the 6-year cumulative incidence and progression of AMD in older adults (≥50 years old) in Nakuru, Kenya.

DESIGN, SETTING, AND PARTICIPANTS This study assessed a population-based cohort with 6-year follow-up of 4414 participants who had a complete assessment. Random cluster sampling with probability proportionate to size procedures was used to select a representative, cross-sectional sample of adults 50 years and older from January 26, 2007, through November 11, 2008. A 6-year follow-up was undertaken from January 7, 2013, through March 12, 2014. On both occasions, a comprehensive ophthalmic examination was performed that included logMAR visual acuity, digital retinal photography, and grading of images at Moorfields Eye Hospital Reading Centre. Data were collected on general health and risk factors.

MAIN OUTCOMES AND MEASURES Incident AMD in participants with no AMD at baseline and progression from early to late AMD.

RESULTS A total of 1453 of the 2900 individuals (50.1%) at risk for AMD were followed up after 6 years (mean [SD] age, 60.7 [8.2] years; 635 female [49.5%]; 799 Kikuyu [62.3%], 324 Kalenjin [25.3%], and 159 other [12.4%]); 1282 had data on AMD status at follow-up. Of these, 202 developed early AMD, and no participants developed late AMD. The 6-year weighted (for loss to follow-up) cumulative incidence of early AMD was 164.2 per 1000 persons (95% CI, 136.7-195.9 per 1000 persons). Two individuals with baseline early AMD from the 142 at risk had developed late AMD at follow-up, with a 6-year cumulative incidence of progression from early to late AMD of 24.5 per 1000 persons (95% CI, 5.0-111.7 per 1000 persons). Cumulative incidence of AMD increased with age (≥80 years old vs 50-59 years old: 1.8; 95% CI, 0.9-3.5) and was higher in women (female vs male: 1.6; 95% CI, 1.2-2.1) and persons with diabetes (diabetes vs no diabetes: 1.7; 95% CI, 1.0-2.8).

CONCLUSIONS AND RELEVANCE In Kenya, more than 100 000 estimated new cases of AMD, mainly early AMD, will develop every year in individuals 50 years or older, although a 50% loss to follow-up and wide CIs for progression to late AMD limit definitive conclusions from these findings.

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Supplemental content

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Age-related macular degeneration (AMD) is a progressive degenerative disease that affects the central retina and is highly associated with age.[1] Advanced AMD, including geographic atrophy (late dry) and neovascular AMD (wet), leads to central vision loss. In the early dry form of the disease, deposits known as drusen are layered between the retina and choroid, and subtypes of drusen (based on size and morphologic features) form part of the more detailed classifications. Although AMD is a leading cause of visual impairment and blindness in populations living in high-income countries,[2] there is a paucity of available data from low- and middle-income countries,[3] including sub-Saharan Africa. However, a systematic review[4] found that overall posterior-segment disease is a common cause of visual impairment in sub-Saharan Africa, and a survey[5] in Kenya found that 1 in 10 persons 50 years and older had signs of AMD.

Estimation of the incidence and progression of AMD and associated sight loss is important for planning of services. Treatment of neovascular AMD is currently possible in well-established health care systems but infrequently available in low- and middle-income countries. It is therefore important to be able to identify individuals at high risk for AMD to consider targeted approaches for prevention and/or treatment. Furthermore, rehabilitation services need to be planned for individuals developing visual loss as a result of AMD. Unfortunately, data to plan these services are currently lacking. The incidence of AMD has been investigated in 7 cohort studies of eye disease worldwide,[6-16] with no data from the African continent. There are large variations in the prevalence, phenotypes, and incidence of AMD in different populations,[6-16] making extrapolation of findings from studies in other regions of the world to an African setting difficult. The aims of the current study were to estimate the 6-year cumulative incidence of AMD in Nakuru, Kenya, and to identify risk factors for incident disease.

Key Points

Question What is the incidence of age-related macular degeneration in Kenya?

Findings A 6-year, population-based cohort study of 4414 adult Kenyans (≥50 years of age) was conducted, and the 6-year weighted cumulative incidence of early age-related macular degeneration was 164.2 per 1000 persons.

Meaning These results suggest that age-related macular degeneration may become a greater public health concern in Kenya and similar countries in the future with population aging in these regions.

Methods

We studied a population-based cohort with 6-year follow-up of 4414 participants who had a complete assessment. Random cluster sampling with probability proportionate to size procedures was used to select a representative, cross-sectional sample of adults 50 years and older from January 26, 2007, through November 11, 2008. A 6-year follow-up was undertaken from January 7, 2013, through March 12, 2014. The following examination protocols were implemented at baseline and follow-up, with detailed methods available elsewhere[17] and in the eMethods in the Supplement. The London School of Hygiene & Tropical Medicine Ethics Committee and the African Medical Research Foundation granted ethical approval for the study, which was also approved by the provincial medical officer for Nakuru County. Written approval was sought from the administrative heads in each cluster, usually the village chief. All participants gave written or thumbprint consent to participate. People requiring medical treatments were referred to the appropriate center. All data were deidentified.

Ophthalmic and General Examination

All participants underwent logMAR visual acuity testing on each eye separately and corrected visual acuity when less than 20/40 Snellen equivalent. Detailed interviews were undertaken in the local language on demographic details, information on risk factors, socioeconomic status, and full medical history. A nurse recorded the blood pressure, weight, height, and waist and hip circumferences. Participants had 2 nonstereoscopic, digital, 45° fundus photographs (1 disc and 1 macula centered) taken per eye by an ophthalmic clinical officer. Digital images were graded at an approved grading center. The senior grader (N.S.) graded all images for the presence of AMD. All eyes classified as having late-stage AMD were adjudicated by the Moorfields Eye Hospital Reading Centre clinician (T.P.). The adjudicator (T.P.) also graded 5% of randomly selected images to ensure quality control.

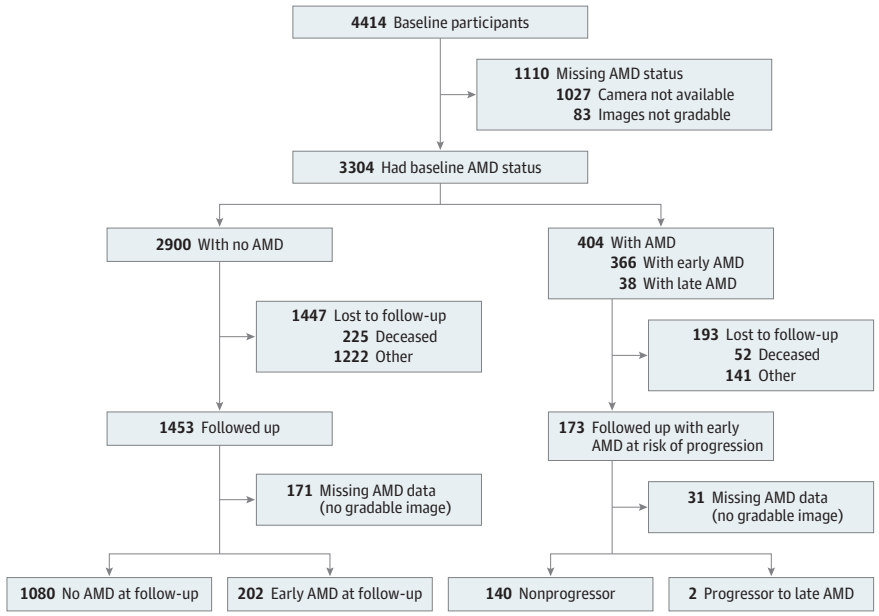
Definitions of AMD Used

A modified version of the international classification and grading system for age-related maculopathy and AMD was used for image grading at baseline and follow-up.[18] Drusen were categorized based on size, uniformity of color, and margins. Patients were classified into hard or soft drusen categories: small drusen (<63 μm) were considered to be hard. Large drusen with a uniform density, sharp margins, and a nodular surface texture were placed in the soft distinct category, whereas those without sharp margins were classified as indistinct. When end-stage disease was apparent, patients were classified as having geographic atrophy in the presence of well-demarcated regions with diameters greater than 175 μm, within which large choroidal vessels were clearly visible to the atrophy of the overlying choriocapillaris and retinal pigment epithelium. Neovascular AMD was graded as present when exudative features, such as serous fluid, hemorrhage, lipid exudates, or fibrosis, were seen to be originating primarily from the subretinal, pigment, and epithelial tissue layers.

Case definitions were based on the eye with more severe status if both eyes were gradable and on the gradable eye if only one was gradable. Early AMD was defined as the presence of large, soft drusen and pigmentation greater than 63 μm, and late AMD was defined as the presence of geographic atrophy or neovascular AMD.

Incident AMD was defined on the basis of the absence of AMD features at baseline on retinal images and the subse-

Figure. Participant Flowchart



AMD indicates age-related macular degeneration.

quent presence of these features at follow-up. Incident late AMD was defined as the combination of no or early AMD at baseline and signs of late AMD at follow-up.

Dealing With Loss to Follow-up

Logistic regressions corrected for the survey design were used to calculate *P* values to assess differences between participants seen and lost to follow-up and those known to have died. An inverse probability weighting (IPW) model was used to allow estimation of cumulative incidence while accounting for those lost to follow-up. Those who had died between baseline and follow-up were excluded from the analysis. Multivariable logistic regression was used to identify independent baseline covariates associated with loss to follow-up. Covariates for which there was evidence of association with the outcome ($P < .10$) were kept in a multivariable model. Individuals without a complete set of the baseline covariates included in the final multivariable model were excluded from any estimations based on the weighted analysis. From this final model, the probability of being followed up was estimated based on the presence or absence of each of these baseline covariates. The inverse of this probability formed the weighting to be applied to account for those lost to follow-up.

The final step was to exclude those individuals lost to follow-up from the analysis and apply the IPW to account for those lost to follow-up. A sensitivity analysis for this approach involved a complete records analysis (ie, including only individuals who had complete records for outcome and all variables in the analysis).

Cumulative Incidence Estimation

The 6-year cumulative incidence of AMD was estimated by dividing the total (weighted) number of individuals who were classified as having AMD at follow-up by the (weighted) number of individuals who were AMD free at baseline and examined at follow-up. The 6-year cumulative incidence was then used to estimate the expected number of new AMD cases per year. The size of the at-risk population in Kenya was estimated using the baseline prevalence of AMD from this cohort and the 2015 Kenyan population estimates for those 50 years or older. The 6-year incidence was then multiplied by this at-risk population and divided by 6, with the assumption that cumulative incidence was constant over time. Annual cumulative incidence was also estimated separately for men and women and in 10-year age categories (50-59, 60-69, 70-79, and ≥80 years). The incidence of progression from early to late AMD was calculated by examining participants with early AMD at baseline who were followed up and had a valid AMD status at follow-up.

Assessing Risk Factors Associated With AMD Incidence

The age-adjusted association between AMD incidence and each covariate was estimated using a Poisson regression model. A multivariable model was created with backward stepwise selection using the likelihood ratio test and a threshold of 2-tailed $P < .05$ for retention of a variable in the model.

Results

At baseline, 4414 participants had a complete assessment, of whom 3304 (74.9%) had an AMD assessment from retinal imaging (**Figure**). Of these participants, 404 (12.2%) had AMD at baseline, with 366 (90.6%) having early AMD and 38 (9.4%) having late AMD. An additional 2900 participants did not have AMD at baseline and were therefore at risk for developing AMD at follow-up.[5]

Table 1. Baseline Characteristics of All 2900 Individuals With No AMD at Baseline According to Availability of AMD Status at 6-Year Follow-up[a]

Baseline Characteristic	Missing Values	Participants	Nonparticipants or Not Included in Analysis	
		Followed Up (n = 1282)	Not Followed Up[b] (n = 1393)	Deceased (n = 225)
Age, mean (SD), y	0	60.7 (8.2)	61.8 (9.8)	68.5 (12.0)[c]
BP, mean (SD), mm Hg				
Systolic	26	138.4 (23.6)	139.3 (23.6)	143.3 (28.7)[c]
Diastolic	26	83.1 (13.0)	82.6 (13.1)	82.4 (16.0)
Random blood glucose level, mean (SD), mg/dL	79	5.2 (2.3)	5.2 (2.2)	5.6 (3.3)[c]
Sex				
Male	0	647 (50.5)	707 (50.8)	86 (38.2)
Female	0	635 (49.5)	686 (49.2)	139 (61.8)[c]
BMI[d]				
Underweight (<18.5)	29	139 (10.9)	188 (13.7)	52 (23.2)[c]
Normal (18.5-24.99)	0	648 (50.7)	674 (49.2)	113 (50.4)
Overweight (25-29.99)	0	307 (24.0)	321 (23.4)	40 (17.9)
Obese (≥30)	0	184 (14.4)	186 (13.6)	19 (8.5)
Vision status impaired, <6/12 better eye				
Normal	18	1233 (96.3)	1279 (93.0)[e]	195 (86.7)[c]
Impaired	0	48 (3.7)	97 (7.0)	30 (13.3)
Tribe				
Kikuyu	0	799 (62.3)	782 (56.1)[e]	152 (67.6)
Kalenjin	0	324 (25.3)	313 (22.5)	52 (23.1)
Other	0	159 (12.4)	298 (21.4)	21 (9.3)
Educational level				
None	21	119 (9.3)	163 (11.9)[e]	15 (6.7)[c]
Primary	0	345 (26.9)	432 (31.4)	91 (40.6)
Secondary	0	677 (52.8)	608 (44.3)	94 (42.0)
Higher	0	140 (10.9)	171 (12.4)	24 (10.7)
Residence				
Rural	0	937 (73.1)	763 (54.8)[e]	161 (71.6)
Urban	0	345 (26.9)	630 (45.2)	64 (28.4)
SES quartile				
Lower	34	266 (20.9)	324 (23.7)[e]	66 (29.5)
Middle lower	0	347 (27.2)	304 (22.2)	55 (24.6)
Middle upper	0	345 (27.1)	342 (25.0)	60 (26.8)
Upper	0	317 (24.9)	397 (29.0)	43 (19.2)
Smoker				
Never	15	861 (67.2)	980 (71.1)[e]	134 (59.6)
Former		104 (8.1)	124 (9.0)	22 (9.8)
Current		317 (24.7)	274 (19.9)	69 (30.7)
Alcohol use				
Never	23	524 (40.9)	512 (37.3)	61 (27.2)[c]
Former	0	549 (42.9)	595 (43.3)	116 (51.8)
Current	0	207 (16.2)	266 (19.4)	47 (21.0)

Abbreviations: AMD, age-related macular degeneration; BMI, body mass index; BP, blood pressure; SES, socioeconomic status.

[a] Data are presented as number (percentage) of participants unless otherwise indicated.

[b] Participants not followed up were alive, unknown, or had AMD status missing.

[c] $P < .05$ for association between the baseline characteristic and the odds of dying during the follow-up period among all participants identified as non-AMD at baseline, excluding the group who were not followed up.

[d] Calculated as weight in kilograms divided by height in meters squared.

[e] $P < .05$ for association between the baseline characteristic and the odds of being followed up among all participants identified as non-AMD at baseline and not known to be deceased at follow-up.

Characteristics of participants and nonparticipants at 6-year follow-up are given in **Table 1**. Nonparticipants were divided into those who had died and those who lived but did not attend the examination clinic (eg, because of mass displacement in the period of postelection violence after the baseline study period) and/or those without a valid AMD assessment (eg, cataract obstructing a view of the retina). Compared with those followed up, participants who had died during follow-up were older and more likely to be female, have lower educational level, have higher systolic blood pressure, and have diabetes but lower body mass index. Compared with participants seen, those lost to follow-up were less likely to be Kikuyu or Kalenjin speakers, had lower levels of education, and were more likely to be from urban areas and from the highest or low-

Table 2. Age- and Sex-Specific 6-Year Cumulative Incidence of Age-Related Macular Degeneration Among the Nakuru Eye Disease Cohort Study Participants

	Males		Females		Overall	
Age Group, y	No. of Cases/No. at Risk	Risk per 1000 at 6 Years (95% CI)	No. of Cases/No. at Risk	Risk per 1000 at 6 Years (95% CI)	No. of Cases/No. at Risk	Risk per 1000 at 6 Years (95% CI)
50-59	29/288	98.2 (64.8-146.1)	60/369	172.7 (129.4-226.6)	89/657	139.3 (105.3-181.9)
60-69	33/221	146.6 (103.6-203.4)	38/197	214.5 (152.0-293.7)	71/418	179.9 (142.8-224.3)
70-79	20/104	184.6 (121.3-270.9)	13/66	193.0 (109.3-318.0)	33/170	188.0 (138.2-250.6)
≥80	4/22	148.1 (51.0-360.0)	5/15	378.8 (132.6-708.7)	9/37	243.8 (115.8-442.4)
All ages	86/635	130.5 (104.1-162.4)	116/647	197.0 (156.7-244.7)	202/1282	164.2 (136.7-195.9)

Table 3. Extrapolated Number of New Adults 50 Years and Older in Kenya Developing Age-Related Macular Degeneration per Year[a]

	Extrapolated No. (95% CI)		
Age Group, y	Males	Females	Overall
50-59	16 460 (10 860-24 500)	31 520 (23 630-41 360)	48 770 (36 890-63 700)
60-69	12 280 (8680-17 040)	21 800 (15 450-29 860)	33 450 (26 540-41 690)
70-79	6650 (4370-9750)	7720 (4370-12 710)	14 550 (10 700-19 400)
≥80	1520 (520-3710)	4550 (1590-8520)	5520 (2620-10 020)
All ages >50	38 280 (30 530-47 650)	65 720 (52 270-81 620)	103 070 (85 800-123 020)

[a] On the basis of incidence data (adjusted for loss to follow-up) and estimates of the population in Kenya by age group in 2015.

est socioeconomic quartile. Individuals seen at follow-up were less likely to have impaired vision at baseline (48 [3.7%]) compared with those who died before follow-up (30 [13.3%]) or those not seen at follow-up (97 [7.0%]).

In total, 1453 persons (50.1%) at risk for AMD were followed up after 6 years (Figure), and 1282 had data on AMD at follow-up. Of these, 202 developed early AMD, and no participants developed late AMD. The 6-year cumulative incidence of early AMD, after taking account of loss to follow-up by using IPW, was 164.2 per 1000 persons (95% CI, 136.7-195.9 per 1000 persons).

In addition, 366 participants with early AMD were at risk of progressing to late AMD at follow-up, of whom 173 were followed up and 142 had a valid AMD assessment (25 of 31 who did not have an AMD assessment had a lens opacity that obscured the retinal images). Two individuals with early AMD from the 142 at risk had developed late AMD at follow-up (Figure), giving a 6-year cumulative incidence of progression from early to late AMD of 24.5 per 1000 persons (95% CI, 5.0-111.7 per 1000 persons).

Of the 38 individuals with late AMD at baseline, 17 (44.7%) were followed up, 5 (13.2%) died, and 16 (42.1%) were not located for follow-up. Of the 17 individuals who were followed up, 4 (23.5%) did not have a valid AMD assessment (because of obstructing lens opacities), 11 (64.7%) remained classified as having late AMD, and 2 (11.8%) had a critical eye that was difficult to grade because of image quality but most likely had stable end-stage AMD. The visual status at baseline and follow-up is given in eTable 1 in the Supplement.

Cumulative incidence of AMD (≥80 vs 50-59 years of age: 243.8 per 1000 persons [95% CI, 115.8-442.4 per 1000 persons] vs 139.3 per 1000 persons [95% CI, 105.3-181.9 per 1000 persons]) strongly correlated with age (**Table 2**). The cumulative incidence of AMD was higher among women than men in each age group (197.0 per 1000 persons [95% CI, 156.7-244.7 per 1000 persons] vs 130.5 per 1000 persons [95% CI, 104.1-162.4 per 1000 persons]), with an overall 6-year cumulative incidence of 197 new cases per 1000 persons (95% CI, 157-245 per 1000 persons) among women compared with 131 new cases per 1000 persons (95% CI, 104-162 per 1000 persons) among men, giving an unadjusted risk ratio of 1.51 (95% CI, 1.14-2.00). For each increase in age category, the risk ratio was estimated to be 1.19 (95% CI, 1.00-1.42).

On the basis of extrapolations of these results to census data and population estimates in 2015 (assuming incident cases annually is proportional to the cumulative incidence), we estimate that, in Kenya, 103 070 new cases of AMD (at any severity) develop every year in persons 50 years or older, of whom 65 720 (63.8%) are women (**Table 3**).

Specific features of AMD that appear or regress during the study period were recorded (eTable 2 in the Supplement). Small drusen were noted to have a 6-year cumulative incidence of 59.1% (95% CI, 53.7%-64.3%) and a cumulative risk of 24.1% (95% CI, 20.6%-28.0%) for regression. Hyperpigmentation and hypopigmentation had a high cumulative risk of resolution during the 6-year follow-up period (hyperpigmentation: 77.0%; 95% CI, 59.5%-88.4%; hypopigmentation: 58.1%; 95% CI, 39.7%-74.4%) but a low incidence (hyperpigmentation: 3.5%; 95% CI, 2.5%-5.0%; hypopigmentation: 5.0%; 95% CI, 3.5%-7.1%).

Multivariable analysis of factors associated with incident AMD indicated an increasing incidence of AMD with older age (P for trend = .02), female sex (P = .001), and diabetes (P = .04) (**Table 4**).

Of the 234 individuals in the cohort who developed incident vision impairment, 162 (69.2%) had an available AMD assessment at follow-up. Of the 162 individuals, 52 (32.1%) had AMD, and 3 of these patients were classified as blind. It was not possible to infer whether vision loss was attributable solely to AMD or a combination of other ocular comorbidities. Change in vision category from baseline to follow-up in all those with

Table 4. Age-Adjusted and Multivariable Analysis of Baseline Covariables and Incident AMD in the Nakuru Eye Disease Cohort Study Sample of 1282 Individuals

Covariable	No. at Risk of AMD[a]	No. With Incident AMD[b]	Risk per 1000 at 6 Years (95% CI)	Age-Adjusted Risk Ratio (95% CI)	Baseline *P* Value	Multivariable-Adjusted Risk Ratio (95% CI)[c]	Baseline *P* Value
Age group, y							
50-59	657	89	139.3 (105.3-181.9)	1 [Reference]	.16	1 [Reference]	.07
60-69	418	71	179.9 (142.8-224.3)	1.3 (1.0-1.7)		1.3 (1.0-1.7)	
70-79	170	33	188.0 (138.2-250.6)	1.4 (0.9-1.9)		1.5 (1.0-2.1)	
≥80	37	9	243.8 (115.8-442.4)	1.8 (0.8-3.7)		1.8 (0.9-3.5)	
Sex							
Male	635	86	130.5 (104.1-162.4)	1 [Reference]	.002	1 [Reference]	.001
Female	647	116	197.0 (156.7-244.7)	1.6 (1.2-2.1)		1.6 (1.2-2.1)	
BMI[d] (4 missing values)							
Underweight (<18.5)	139	25	191.3 (127.2-277.4)	1 [Reference]	.84	NA	NA
Normal (18.5-24.99)	648	98	160.1 (129.9-195.7)	0.8 (0.5-1.3)		NA	
Overweight (25-29.99)	307	49	159.4 (113.0-220.1)	0.9 (0.6-1.4)		NA	
Obese (≥30)	184	30	169.1 (119.0-234.6)	0.9 (0.6-1.6)		NA	
Location							
Rural	937	146	160.0 (131.9-192.8)	1 [Reference]	.55	NA	NA
Urban	345	56	171.2 (116.8-244.0)	1.1 (0.8-1.7)		NA	
SES quartile (7 missing values)							
Lower	266	50	216.0 (154.0-294.2)	1 [Reference]	.07	NA	NA
Lower middle	347	43	128.5 (94.4-172.4)	0.6 (0.4-0.9)		NA	
Upper middle	345	59	169.1 (128.1-219.8)	0.8 (0.5-1.3)		NA	
Upper	317	48	148.5 (105.9-204.4)	0.7 (0.5-1.1)		NA	
Smoker							
Never	861	142	173.6 (141.6-211.1)	1 [Reference]	.12	NA	NA
Former	104	9	83.5 (39.5-167.9)	0.5 (0.2-1.0)		NA	
Current	317	51	165.7 (125.5-215.7)	0.9 (0.7-1.2)		NA	
Hypertension (2 missing values)							
No	664	95	149.1 (113.3-193.6)	1 [Reference]	.37	NA	NA
Yes	616	106	178.0 (143.1-219.2)	1.2 (0.8-1.6)		NA	
Diabetes (1 missing value)							
No	1223	188	157.8 (131.7-187.9)	1 [Reference]	.07	1 [Reference]	.04
Yes	58	14	263.9 (136.3-448.9)	1.7 (1.0-2.8)		1.7 (1.0-2.8)	
Alcohol use (2 missing values)							
Never	524	85	171.6 (133.7-217.5)	1 [Reference]	.59	NA	NA
Former	549	81	155.2 (117.5-202.2)	0.8 (0.6-1.2)		NA	
Current	207	36	169.6 (116.3-240.6)	1.0 (0.6-1.4)		NA	
Ethnic group							
Kikuyu	799	126	164.7 (130.5-205.6)	1 [Reference]	.51	NA	NA
Kalenjin	324	46	148.5 (107.4-201.7)	0.9 (0.6-1.3)		NA	
Other	159	30	184.4 (119.2-274.3)	1.2 (0.8-2.0)		NA	
Educational level (1 missing value)							
No education	119	12	111.3 (58.2-202.5)	1 [Reference]	.16	NA	NA
Primary	345	66	215.8 (161.8-281.7)	1.8 (0.9-3.4)		NA	
Secondary	677	104	152.8 (123.7-187.4)	1.3 (0.7-2.5)		NA	
College or university	140	20	128.5 (80.7-198.4)	1.2 (0.5-2.6)		NA	

Abbreviations: AMD, age-related macular degeneration; BMI, body mass index; NA, not applicable; SES, socioeconomic status.

[a] At risk indicates no AMD at baseline.

[b] Incident AMD indicates early or late AMD at follow-up.

[c] For multivariable analysis, an initial model was fitted that included those variables associated with outcome in age-adjusted analysis (using a Wald test threshold $P < .05$ to indicate association). A backward stepwise approach was then applied to obtain a final multivariable model, removing variables with $P > .05$ one by one.

[d] Calculated as weight in kilograms divided by height in meters squared.

a valid AMD status at baseline and follow-up is given in eTable 3 in the Supplement.

A total of 202 participants in the cohort developed incident AMD, of whom 192 (95.0%) had normal vision at baseline. A total of 27 (14.1%) of the 192 developed visual impairment by follow-up. A total of 1080 participants did not develop AMD, with 1040 (96.3%) in this group having normal vision at baseline. Of these 1040 individuals, 83 (8.0%) developed vision impairment.

Discussion

The Nakuru Eye Disease Cohort Study provides longitudinal data on AMD in sub-Saharan Africa from a population-based cohort. Although there is 50% loss to follow-up and few cases of late AMD (resulting in wide CIs for that outcome), there are limited data on these outcomes from this region. With those caveats in mind, during 6 years, 1 in 6 adults 50 years or older developed early manifestations of AMD, with women having a higher incidence than men. Increasing age was strongly related to the prevalence and incidence of AMD. Most incident cases of AMD were defined on the basis of the development of large drusen (>64 μm). Late AMD was infrequent at baseline, and consistent with this pattern, only 2 cases of incident late AMD were found at follow-up. Both incident cases developed in individuals with early AMD at baseline, and no case was identified that progressed from no AMD to late AMD.

Our data estimate a higher incidence of AMD than other (non-African) cohort studies of eye disease (eTable 4 in the Supplement). A likely explanation is that the Nakuru cohort includes only persons 50 years or older, similar to the next 2 highest cumulative annual incidence estimates, which were also from samples of older individuals in Copenhagen[6] and Reykjavik.[11] Furthermore, in the Nakuru study, there was a higher incidence of early AMD and a lower incidence of late AMD compared with other populations. This observation is consistent with the baseline finding, which indicated a comparatively high prevalence of early AMD but low prevalence of late AMD.[5-16] The 2 participants who progressed from early to late AMD were older than 80 years; the reduced number of individuals in this age group in the Nakuru cohort may explain the low incidence of late AMD because age is the leading risk factor for incident AMD.

A high prevalence of early AMD at baseline and a high incidence of early AMD at follow-up may suggest that the population under investigation has a higher risk of developing AMD. The relatively high prevalence and incidence may possibly be attributed to greater UV light exposure, earlier biological aging, greater genetic predisposition, or greater susceptibility to inflammatory processes, which have been attributed to AMD.[19] The proportion of persons with vision loss attributable to AMD is relatively low because overall vision loss primarily attributable to conditions such as cataract is largely under control in more developed health care systems. Of those with AMD, 14% developed vision impairment during the 6-year study period compared with 9% during 14 years in a well-developed health care system in Copenhagen. However, vision impairment cannot be attributed to AMD alone.

Strengths and Limitations

This study was conducted under challenging circumstances with limited infrastructure. It provides independently graded, digital image-based analysis of AMD in an East African cohort that is diverse and largely representative of the population from which it was sampled. Detailed ophthalmic, demographic, and anthropometric assessment of each participant has enabled valuable analyses of associations and risk factors.

Despite these strengths, limitations of the current study may have contributed to an underestimation of the true incidence of AMD and AMD lesions. First, the main limitation of our study is the large loss of participants at follow-up. Of the 4414 persons who participated in the baseline study, only 2171 persons participated in the follow-up examination, of whom 1424 had gradable images at baseline and follow-up, with most being excluded from analysis as a result of camera failure at baseline, lack of electricity access, and/or ungradable images attributable to media opacities. Only those who had gradable images at both time points were included in the analysis. A complete case record analysis was conducted without weighting for loss to follow-up (eTable 5 in the Supplement), with results similar to those using the IPW modeling (Table 2), with a possible underestimation of the incidence in women when loss to follow-up is not taken into account.

Second, changes in procedures between the baseline and follow-up examination (different retinal camera) may have introduced bias. Change in cameras may have caused images with different color profiles and saturation levels, resulting in different abilities to detect AMD features (eg, drusen and pigment). Furthermore, the lack of stereophotographs meant cases of retinal elevation may have been overlooked. These factors may have resulted in bias toward an underestimation of the incidence of subtle early AMD lesions, such as small drusen, or an overestimation of pigmentation attributed to AMD. Comparison images between cameras of the same study participants at baseline and follow-up are given in eTable 6 in the Supplement. Overall image quality was considered to be equivalent at the 2 time points in those with clear media (ie, no lens or corneal opacity).

Third, survival bias may have caused an underestimation of the true incidence of late AMD if those who died before the follow-up had experienced advanced AMD lesions after the first examination, and it is possible that those with worsening disease were more likely to attend follow-up visits. The low prevalence of late AMD at baseline and low incidence can, in part, be attributed to a lack of older individuals in this study population, with an expected shorter life span than other populations with data on AMD incidence. Classification bias may also have contributed to the estimates, and histologic studies would be required to confirm whether the manifestations being attributed to AMD are consistent with those in other populations.

Conclusions

We estimate that, in Kenya, more than 100 000 new cases of AMD, mainly early AMD, will develop every year in persons 50 years and older, although a 50% loss to follow-up and wide CIs for progression to late AMD limit definitive conclusions from these findings. The AMD in this population was found to be phenotypically different from that in a prior study.[5] However, because the relatively high incidence was restricted to occurrence of early AMD, the high incidence of early AMD may not have major implications for clinical practice given the low number of individuals with associated visual loss.

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Supplementary Online Content

Bastawrous A, Mathenge W, Peto T, et al. Six-year incidence of age-related macular degeneration in Kenya: Nakuru Eye Disease Cohort Study. *JAMA Ophthalmol.* Published online May 11, 2017. doi:10.1001/jamaophthalmol.2017.1109

This supplementary material has been provided by the authors to give readers additional information about their work.

eMethods. Ethics Statement, Sampling Strategy, and Inverse Probability Weighting

Ethics Statement

The London School of Hygiene & Tropical Medicine (LSHTM) Ethics committee and the African Medical Research Foundation (AMREF) granted ethical approval for the study and by the Provincial Medical Officer for Nakuru County. Written approval was sought from the administrative heads in each cluster, usually the village chief. All participants gave written or thumbprint consent to participate. People requiring medical treatments were referred to the appropriate centre.

Sampling Strategy and Recruitment

The study baseline fieldwork was carried out at baseline between January 2007 and November 2008. The follow-up study took place between October 2012 and March 2014.

At baseline, 100 clusters were selected across Nakuru County with a probability proportional to the size of the population using the electoral roll as the sampling frame. A cluster was defined as the area served by a polling station. Households were selected within clusters using a modified compact segment sampling method.[1] Each cluster was divided into segments so that each segment included approximately 50 people aged ≥50 years. One segment was selected at random, and all eligible people were included sequentially until 50 had been examined.

The sample size of 5000 people at baseline (2007-2008) was sufficient to estimate a prevalence of AMD of 3.0% among those aged ≥50 years, with a required precision of 0.5%, 95% confidence, a design effect to account for clustering of 1.5, and a response rate of 90%. (Epi Info 6.04, Centers for Disease Control and Prevention, Atlanta, GA). In total, 4,381 participants were recruited at baseline (response rate 81%).

All participants were invited to attend an examination clinic at a central location within the cluster (see below).

Follow-up

One week before the follow-up examination clinic was carried out a field officer studied the maps of the village including GPS coordinates recorded at baseline and made phone contact with the village chief or guide to arrange a planning visit. A list of study participants were given to the chief and a local village guide was recruited to assist locating the study participants. On the day prior to the examination clinic, a study team visited homes of baseline participants and confirmed their identity using National Identity cards and invited them to attend the examination clinic the following day.

On the examination day, the advance team confirmed the identity of participants against data from baseline (age, date of birth, name, and identity cards). In cases of uncertain identity, confirmation was made based on retinal examination verified by comparison of retinal photos with baseline photo (n=12).

Visual Acuity

All participants underwent visual acuity (VA) testing on each eye separately at four meters using a reduced LogMAR tumbling 'E' chart[2] in a well illuminated area as described elsewhere.[3,4] Presenting VA was defined as the number of letters read correctly without glasses if the participant did not have glasses or with glasses if they had them.

All participants underwent Autorefraction and those with a presenting acuity of <24 LogMAR letters (<20/40 Snellen Equivalent) had a corrected VA assessed in addition to presenting (uncorrected, under corrected or corrected). More detailed methodology is available elsewhere.[5]

Fundus photography

The participants had two non-stereoscopic digital 45^0 fundus photographs taken per eye by an ophthalmic clinical officer using a TRC-NW6S Non-Mydriatic Retinal Camera with 10 megapixel Nikon D80 (Top Con®) at baseline and a DRS CentreVue+ (Haag-Streit) Retinal Camera at follow-up. One image was centred on the optic disc while the other was centred on the macula. The digital images were forwarded to the Retinal Grading Centre at Moorfields Eye Hospital Reading Centre (MEHRC) London for grading and confirming the clinical diagnosis of posterior segment disease.

Questionnaire and anthropometry

Detailed interviews were undertaken in the local language covering demographic details, information on risk factors, socio-economic status (SES) and full past medical history. SES was evaluated using a continuous asset score, which was produced for each participant, using a scoring system derived through principal component analysis in an earlier study in this setting.[6,7] The scale included assessment of 17 asset items and five measures of household characteristics.

A nurse recorded the blood pressure of participants three times on the right arm of the participant, at least five minutes apart after an initial period of five minutes of rest using the Omron digital automatic monitor (model HEM907). Weight was measured to the nearest kilogram using standard scales (Seca 761 scales) after the participant had removed all heavy clothing and shoes. Height was measured to the nearest centimetre while the participant stood without shoes using a standardized stadiometer (Leicester Height Measure). For weight and height the average of two readings was recorded. Waist and hip circumferences were measured with a tape to the nearest centimetre.

Image Grading

The senior grader (NS) graded all images for the presence of AMD. All images were first categorized for quality as excellent, good, fair, borderline and ungradeable. All questionable lesions and all eyes classified as having late-stage AMD were adjudicated by the MEHRC clinician (TP). Any lesions considered to be due to other causes such as myopia and inflammatory disease were not graded for AMD, and these were also verified by TP. The adjudicator also graded 5% of randomly selected images to ensure quality control. Data were single entered onto Excel and checked for consistency by an independent data monitor from MEHRC who was not involved in the study.

Data Handling & Statistical Analyses Methods

Data entry

Image data were double entered into a specially developed dataset (EpiData Entry v2.1). Consistency checks were performed each evening and inconsistencies corrected the same day.

Data analysis

Individuals in the study who were classified as AMD free at baseline were defined as being at risk of developing AMD during the follow-up period of the study.

Inverse Probability Weighting

Of the 2900 individuals at risk of AMD at baseline, 225 were confirmed as deceased during the follow up period. This left 2675 individuals eligible for follow up. Of these 1393 (52%) did not have a valid AMD status at follow up, leaving 1282 individuals eligible for inclusion in the incidence study. To take account for any bias due to this loss to follow up, inverse probability weights were estimated for individuals who

were not confirmed as deceased, then this weighting was applied to the estimates of incidence.

Variables found to be associated with loss to follow up were: age group, residence, socio-economic status, smoking status, alcohol status, tribe, education level and baseline diabetes status. Of those that were followed up, socio-economic status was missing for 7 individuals. So these individuals were excluded from the weighted estimates, as the number missing was small and socio-economic status was a strong predictor of missingness.

eTable 1. Change in Presenting Visual Acuity Category in Those With Late AMD at Baseline in Those With an AMD Status Available at Both Time Points

		Follow-up					
		Normal	**Mild VI**	**Mod VI**	**Severe VI**	**Blind**	**Total**
Baseline	**Normal**	2	4	1	0	0	7
	Mild VI	0	0	0	0	0	0
	Mod VI	0	0	4	2	3	9
	Severe VI	0	0	0	0	0	0
	Blind	0	0	0	0	1	1
	Total	2	4	5	2	4	17

The proportion in brackets after each number is the proportion that report either baseline or incident AMD (total N=17).

eTable 2. Incidence of Appearance and Regression of Individual Features of AMD Between Baseline and Follow-up

	Feature measured at baseline and follow up (n)	Feature absent at baseline (n)	Feature present at follow-up (n)	6 year cumulative incidence of feature appearance (Adjusted for LTFU using IPW)	Feature present at baseline (n)	Feature absent at follow-up (n)	6 year cumulative incidence of feature regression (Adjusted for LTFU using IPW)
Small drusen	1220	446	261	59.1% (53.7%,64.3%)	774	188	24.1% (20.6%,28.0%)
Large drusen	1134	1039	196	19.6% (16.3%,23.5%)	95	8	6.8% (3.3%,13.5%)
GA	1083	1077	1	0.3% (0.0%,2.0%)	6	1	19.2% (0.7%,89.2%)
CNV	1083	1075	2	0.2% (0.0%,0.7%)	8	2	24.6% (3.4%,75.4%)
Hyperpigmentation	1090	1050	36	3.5% (2.5%,5.0%)	40	30	77.0% (59.5%,88.4%)
Hypopigmentation	1088	1053	48	5.0% (3.5%,7.1%)	35	21	58.1% (39.7%,74.4%)
RPE detachment	1081	1080	0	-	1	1	100.0%

LTFU: Loss to follow-up, IPW: Inverse Probability Weighting

eTable 3. Change in Presenting Visual Acuity Category From Baseline to Follow-up in Cohort With Visual Acuity Data and AMD Status Available at Both Time Points

		Follow-up					
		Normal	**Mild VI**	**Mod VI**	**Severe VI**	**Blind**	**Total**
Baseline	**Normal**	1,058 (21.6%)	153 (30.7%)	103 (35.0%)	0 (N/A)	3 (66.7%)	1,317 (23.8%)
	Mild VI	13 (23.1%)	16 (31.3%)	22 (31.8%)	0 (N/A)	0 (N/A)	51 (29.4%)
	Mod VI	9 (33.3%)	9 (55.6%)	34 (41.2%)	7 (42.9%)	1 (0.0%)	60 (41.7%)
	Severe VI	0 (N/A)	0 (N/A)	2 (50.0%)	0 (N/A)	0 (N/A)	2 (50.0%)
	Blind	0 (N/A)	0 (N/A)	1 (100.0%)	0 (N/A)	4 (50.0%)	5 (60.0%)
	Total	1,080 (21.7%)	178 (32.0%)	162 (36.4%)	7 (42.9%)	8 (50.0%)	1,435 (24.9%)

The proportion in brackets after each number is the proportion that report either baseline or incident AMD (total N=1,435)

eTable 4. Population-Based Cohort Studies of AMD

Study	Location	Year commenced	Years of Follow up	No of participants	Age at Baseline	Cumulative incidence of Early AMD (%)	Cumulative annual incidence of Early AMD (%)*	Cumulative (study period) Incidence of Late AMD (%)**	Reference
Nakuru	Kenya	2007	Baseline 6	4414 2171	50+	16.4	2.9	0.2	This paper
Studies of equivalent age groups									
Blue Mountain Eye Study	Australia	1992	Baseline 5 10	3654 2335 1952	49+	14.1	1.4	3.7	[8]
Reykjavik Eye Study	Iceland	1996	Baseline 5	1045 846	50+	10.7	2.1		[9]
Studies of different age groups									
Beaver Dam Eye Study	USA	1988	Baseline 5 10 15	4926 3684 2764 2119	43-86	12.1 14.3	1.0	2.1 3.1	[10-12]
Copen	Den	1986	Base	946	60-				[13]

hagen City Eye Study	mark		line 14	359	80	31.5	2.3	14.8	
Barbados Eye Study	Barbados	1987	Baseline 4 9	4631 3427 2793	40+	5.2 12.6	1.4	Negligible 0.7	[14,15]
Hisayama Study	Japan	1998	Baseline 5 9	1482 961 1401(>40yrs)	40+	8.5 10.0	1.1	0.8 1.4	[16,17]
Los Angeles Latino Eye Study	USA	2000	Baseline 4	6357 4658	40+	7.5	1.9	0.2	[18]

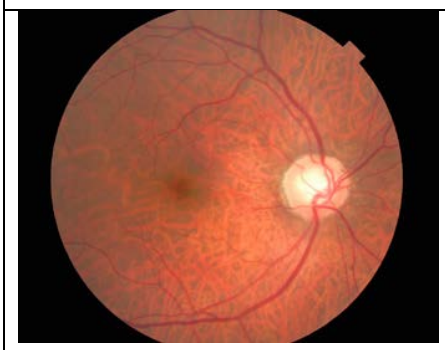
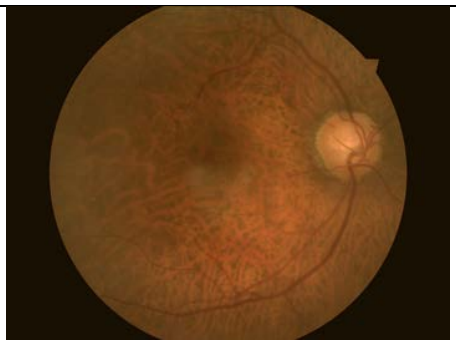
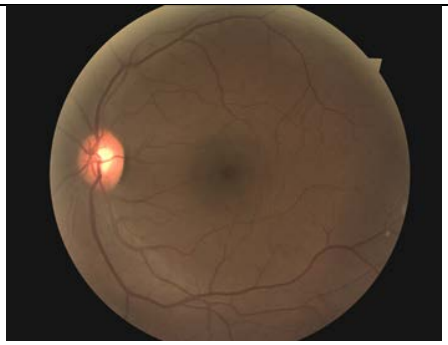
*Annual cumulative incidence is calculated as the overall cumulative incidence divided by the number of years of follow up, where more than one follow-up visit was conducted, the longest one is used.

**Incident Late AMD considered as those without Late AMD (no AMD or Early AMD at baseline).

eTable 5. Unweighted for Missing Data (Complete Case Records Only) Age-and Sex-Specific 6-Year Cumulative Incidence of AMD Among the Nakuru Eye Disease Cohort Study Participants

	Male		Female		Overall	
Age Group (years)	N (Cases / at risk)	Risk per 1,000/6yrs (95%CI)*	N	Risk per 1,000/6yrs (95%CI)*	N	Risk per 1,000/6yrs (95%CI)*
50-59	29 / 288	100.7(66.0,150.7)	60 / 369	162.6(123.5,211.1)	89 / 657	135.5(103.5,175.3)
60-69	33 / 221	149.3(107.2,204.2)	38 / 197	192.9(141.9,256.7)	71 / 418	169.9(137.6,207.9)
70-79	20 / 104	192.3(128.5,277.7)	13 / 66	197.0(113.2,320.4)	33 / 170	194.1(144.8,255.2)
80+	4 / 22	181.8(70.6,394.0)	5 / 15	333.3(137.5,610.6)	9 / 37	243.2(131.3,406.0)
All ages	86 / 635	135.4(108.0,168.5)	116 / 647	179.3(145.3,219.2)	202 / 1282	157.6(132.3,186.6)

eTable 6. Side by Side Image Comparison Between Baseline and Follow-up

Baseline – TopCon NRW6	Followup – Haag Streit DRS CentreVue
	
	

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Chapter 10. Glaucoma features in an East African population: a six-year cohort study of older adults in Nakuru, Kenya

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SECTION A – Student Details

Student	Andrew Bastawrous
Principal Supervisor	Hannah Kuper
Thesis Title	The Nakuru Eye Disease Cohort Study

If the Research Paper has previously been published please complete Section B, if not please move to Section C

SECTION B – Paper already published

Where was the work published?			
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Where is the work intended to be published?	TBC
Please list the paper's authors in the intended authorship order:	Andrew Bastawrous, Wanjiku Mathenge, John Nkurikiye, Tunde Peto, Hillary Rono, Michael Gichangi, Helen A. Weiss, David Macleod, Allen Foster, Matthew Burton, Hannah Kuper
Stage of publication	Final draft complete - ready for review by co-authors then submission for peer-review

SECTION D – Multi-authored work

For multi-authored work, give full details of your role in the research included in the paper and in the preparation of the paper. (Attach a further sheet if necessary)	Study design, data collection, analysis, write up, review, overall lead.

Student Signature: _____ **Date:** 12, April 2017

Supervisor Signature: _____ **Date:** 12, April 2017

Glaucoma features in an East African population: a six-year cohort study of older adults in Nakuru, Kenya

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Abstract

Background

Glaucoma is a leading cause of blindness in low and middle-income countries with people of African descent being at higher risk of early onset glaucoma and subsequent vision loss. Minimal data is available from African population-based cohort studies. The primary aims of this study were to describe the normative distribution of glaucoma features to enable glaucoma classification and to assess risk factors for those with glaucoma at follow-up among people aged ≥50 years in Kenya.

Methods

Random cluster sampling with probability proportionate to size was used to select a representative cross-sectional sample of adults aged ≥50 years in 2007-8 in Nakuru District, Kenya. A six-year follow-up was undertaken in 2013-14. On both occasions a comprehensive ophthalmic examination was performed including LogMAR visual acuity, digital retinal photography, visual fields, intraocular pressure, anterior chamber OCT and independent grading of optic nerve images. Data were collected on general health and risk factors. We report glaucoma features, prevalence and predictors for glaucoma based on the ISGEO criteria at follow-up. These measures were estimated for each covariate using a Poisson regression model with robust error variance to allow for the clustered design and including inverse-probability weighting for loss to follow up.

Results

At baseline, 4,414 participants aged ≥50 years underwent examination. Anterior chamber OCT findings: mean anterior chamber angle of 36.6°, mean central corneal thickness of 508.1µm and a mean anterior chamber depth of 2.67mm. 2,171 participants were examined at follow-up. Only five eyes (0.2%) having occludable angles based on Scheie grading using gonioscopy. The mean baseline IOP in those examined at baseline and follow up was 15.4mmHg and 14.6mmHg in the right and left eyes, respectively. The VCDR distribution based on images in those with normal visual fields at follow up was 0.7 and 0.8 at the 97.5th and 99.5th percentiles, respectively. A total of 88 (4.3%, 95% CI, 3.5-5.9%) of participants at follow-up had glaucoma consistent with ISGEO criteria. A RAPD and raised IOP were associated with the diagnosis.

Conclusions

Glaucoma is a challenging disease to diagnose and treat in low-resource settings and it remains a public health concern with the lack of cost-effective treatments Further research in to the natural history and risk for progression of glaucoma in Africa is required, as well as the development and testing of treatment modalities.

Introduction

Glaucoma is a leading cause of blindness globally. [1] The proportion of the worldwide magnitude of blindness attributable to glaucoma increased by 50% between 1990 and 2010 from 4.4% to 6.6%.[2] This trend is expected to continue over coming decades, with the estimated numbers with glaucoma predicted to rise from 60.5 million people in 2010 to 79.6 million by the year 2020 [3] and then to 111.8 million by 2040 [4] Glaucoma is the second most common cause of blindness in sub-Saharan Africa (SSA), [5] with estimates suggesting that there were 6.5 million people with glaucoma in SSA in 2010 projected to increase to 8.4 million by 2020, though data are sparse.[6]

Whilst blindness from glaucoma may be preventable, this is dependent upon early diagnosis and delivery of long-term effective treatment. Glaucoma poses a particular problem in sub-Saharan Africa due to both higher age-specific prevalence, higher risk for open-angle glaucoma, [7-10], late presentation [11] and low levels of coverage and adherence with treatment. [12, 13] Adherence to topical treatment is sufficiently poor that the primary treatment of choice in SSA is often surgery [5] in the hope that a single intervention achieves long term control of intra-ocular pressure (IOP) as the main modifiable risk factor. [11-13] Furthermore, clinical features of glaucoma may be different in a sub-Saharan African setting compared to elsewhere, necessitating different therapeutic approaches.

The objectives of this study were therefore, within the context of a population-based cohort study in Nakuru, Kenya: i) to describe normative features of glaucoma in this cohort, ii), to describe the prevalence of glaucoma or specific glaucoma features at baseline and at follow up, iii) to assess baseline risk factors for having

glaucoma at follow up and iv) to describe clinical signs predictive of glaucoma at follow up. [14] The distribution of key features of glaucoma (optic nerve morphology, intraocular pressure, visual acuity, angle morphology) and the risk factors associated with changing optic disc morphology that occurred over the six year follow up period will also be described.

Methods

Ethics Statement

The London School of Hygiene & Tropical Medicine (LSHTM) Ethics committee and the African Medical Research Foundation (AMREF) granted ethical approval for the study. Approval was also granted by the Provincial Medical Officer for Nakuru County. Written approval was sought from the administrative heads in each cluster, usually the village chief. All participants gave written or thumbprint consent to participate. People requiring medical treatments were referred to the appropriate health care service.

Sampling Strategy and Recruitment

The study baseline fieldwork was carried out between January 2007 and November 2008. The follow-up study took place between October 2012 and March 2014. At baseline, 100 clusters were selected across Nakuru County with a probability proportional to the size of the population using the electoral roll as the sampling frame. A cluster was defined as the area served by a polling station. Households were selected within clusters using a modified compact segment sampling method [15]. Each cluster was divided into segments so that each segment included approximately 50 people aged ≥50 years. One segment was selected at random, and all eligible people were included sequentially until 50 had been examined.

The sample size of 5000 people was sufficient to estimate a prevalence of disease at 3.0% among those aged ≥50 years, with a required precision of 0.5%, 95% confidence, a design effect to account for clustering of 1.5, and a response rate of 90% (Epi Info 6.04, Centers for Disease Control and Prevention, Atlanta, GA). In

total, 4,381 participants were recruited at baseline (response rate 81%). All participants were invited to attend an examination clinic at a central location within the cluster (see below).

Follow-up

Approximately one week before the follow-up examination clinic was carried out for a given cluster, a field officer studied the maps of the village including GPS coordinates recorded at baseline and made phone contact with the village chief or guide to arrange the visit. At the planning visit a list of study participants were given to the chief and a local village guide was recruited to assist locating the study participants. Two days prior to the clinic, the field officer reminded chiefs of the visit by phone and notified them and the guide of the advance team's arrival. On the day prior to the examination clinic, a study team visited homes of baseline participants and confirmed their identity using National Identity cards and invited them to attend the examination clinic the following day. All identified participants were also asked to help locate baseline participants that had not been found.

On the examination day, the advance team confirmed the identity of participants against data from baseline (age, date of birth, name, and identity cards). In cases of uncertain identity, confirmation was made based on retinal examination verified by comparison of retinal photos with baseline photo (n=12).

In both baseline and follow-up, an examination clinic was established at a central location where there were appropriate amenities such as electricity, water and road access. The following examination protocols were implemented at both baseline and follow-up. [14, 16]

Ophthalmic and General Examination

Visual Acuity

All participants at baseline and follow-up underwent visual acuity testing on each eye separately at four meters using a reduced LogMAR tumbling 'E' chart [17] in an appropriately illuminated area, as described elsewhere.[18, 19] The presenting visual acuity was defined as the number of letters read correctly without glasses if the participant did not have glasses, or with glasses if they had them.

Anterior Segment Examination

At baseline the anterior segment assessment was made on the slit lamp by a single ophthalmologist (WM). The Van Herick angle assessment was performed. [20]

Anterior Chamber OCT

Gonioscopic assessment of the angle was not undertaken, however a Heidelberg Slit Lamp-adapted Optical Coherence Tomography (SL-OCT) (Heidelberg Engineering, Heidelberg, Germany) was used at baseline to examine the anterior segment to provide population normative data on the Angle Opening Distance (AOD), Anterior Chamber Angle (ACA), Central Corneal Thickness (CCT) and Anterior Chamber Depth (ACD). These normative data analyses excluded eyes that were pseudophakic. Furthermore, eyes with trachomatous or non-trachomatous corneal opacities and those with disorganized globes (phthisis, staphyloma) were excluded

from the corneal thickness analysis. All measurements were obtained from scans using the interactive distance measurement of the SL-OCT proprietary software (Heidelberg Eye Explorer v1.5.9.0; Heidelberg Engineering, Heidelberg, Germany). Analyses based on naso-temporal (horizontal) meridians. Anterior chamber depth was assessed using peaks of the corneal reflectivity profile to identify the central cornea as well as the anterior and posterior boundaries of the cornea. Calipers were aligned from the posterior border of the central cornea. Two measurements were averaged for each eye. Anterior chamber angle opening distance was taken as posterior cornea and opposite peripheral iris with the apex lying in the angle recess. All anterior segment measurements were taken with the pupil undilated.

Gonioscopy

At follow-up, an assessment of the opening angle of participants' right and left eyes using direct visualisation was made using a four-mirror gonioscopy lens (Zabbys). This lens does not require coupling fluid and was chosen to minimize impact on the quality of retinal photographs. Angles were recorded using standard Shaffer grading and further classified as "open", "occludable" or "closed" based on standard referral criteria. [21] Angle OCT was not performed at follow-up. Occludable angles were defined at follow up as: pigmented trabecular meshwork not visible in 3⁄4 or more of angle circumference in primary position without manipulation, in presence of low illumination. If the patient could not cooperate with gonioscopy, the Van Herick (VH) technique [20] was used for grading with an anterior chamber depth of less than quarter of the corneal thickness being considered occludable.

Intraocular Pressure (IOP)

At baseline and follow-up participant's eyes were anesthetized using tetracaine 1% eye drops (Kenya Society for the Blind, Eye Drop Production Unit, Nairobi, Kenya) and the tear film stained with fluorescein-impregnated paper. IOP was measured using a Goldmann Applanation Tonometer. One reading was taken from each eye and analysed independently. The tonometer was checked for calibration weekly and disinfected between patients.

Visual Field Assessment

At baseline, all individuals with suspect or abnormal discs on clinical slit-lamp examination underwent automated visual field testing. The Humphrey® Field Analyzer II - 720*i* series (Carl Zeiss Ophthalmic Systems, Inc.) was used. A suspect or abnormal disc was defined as a vertical cup to disc ratio (VCDR) of 0.7 or above; optic disc cupping asymmetry between the eyes of more than 0.2 VCDR; or any other abnormal features including notching, disc haemorrhages or disc pallor. A random sample of five individuals per cluster (10%) also underwent visual field testing to provide normative data.

Participants performed the Swedish Interactive Thresholding Algorithm (SITA) STANDARD 24-2. SITA Fast was used to determine the threshold level in all participants having visual field analysis. Appropriate corrective lenses for refractive errors were used when needed. An automated fixation monitor was used throughout. If the SITA fast test was reliable the SITA standard test was performed. If the SITA fast was unreliable (false-positives, ≥20%; false-negatives, ≥33%; fixation

losses, ≥33%), then this was repeated once. If it remained unreliable then no further testing was done.

At follow-up, a different strategy for visual field testing was used due to challenges at baseline: All subject's eyes with VA equivalent to >=6/60 Snellen underwent automated visual field testing by a trained visual field technician using the Henson 8000 Visual Field Analyser (TopCon, Inc.) The multiple stimulus suprathreshold test was used following manufacturers guidelines (Screening test - 26 test locations). When one or more spots were missed, the 26-point test was repeated for that eye. If any missed spots re-occurred on the second time of testing the test for that eye was extended to 68 test locations. This machine and strategy were used in preference to the baseline methods due to feedback from both patient's and tester at baseline as well as unreliable visual field data from baseline. Patient's found the baseline testing protocol difficult to understand and the time required to complete the test meant only a sub-sample of the population could be investigated.

Visual fields were considered consistent with glaucoma at baseline and follow-up if:

(1) The test was reliable according to performance indices

(2) The glaucoma hemifield test was outside normal limits, and

(3) The test showed three or more abnormal contiguous points clustering in the same hemi field.

Visual Fields were graded at the Moorfields Eye Hospital Reading Centre.

Fundus photography and grading

The participants had two non-stereoscopic digital 45° fundus photographs taken per eye by an ophthalmic clinical officer using a TRC-NW6S Non-Mydriatic Retinal Camera with 10 megapixel Nikon D80 (TopCon®) at baseline and a DRS CentreVue+ (Haag-Streit) Retinal Camera at follow-up. One image was centered on the optic disc while the other was centered on the macula.

The digital images were forwarded to the Retinal Grading Centre at Moorfields Eye Hospital Reading Centre (MEHRC) London for grading and confirming the clinical diagnosis of posterior segment disease.

The senior grader graded all discs considered abnormal on clinical examination at the slitlamp at baseline and all optic nerve images at follow-up. Images were first categorized for quality as excellent, good, fair, borderline or ungradeable. They were then graded for vertical cup disc ratio (VCDR). The scleral ring was identified to determine the margins of the disc and delineating the rim identified the cup. The rim was defined as the area between the border of the optic disc and the position of blood vessel bending and the area within the rim as the cup. A vertical measure of both the cup and disc were taken to calculate the VCDR. Discs images were also examined for any abnormality and were graded as normal, suspicious or abnormal. A disc was deemed abnormal if any of neuro-retinal rim (NRR) thinning, notching or disc hemorrhage(s) were present, if VCDR was ≥0.7. A suspicious disc was one where adjudication was necessary to determine if its appearance was abnormal.

In case of difficulties, the adjudicator (TP) decided on the grading of the images. The adjudicator also graded 5% of randomly selected images to ensure quality control.

At baseline only a subset (10%) of optic discs were graded based on images with all participant's receiving a clinical slit lamp grading and estimation of VCDR. At follow-up, all participants' discs were estimated based on image grading.

Data Handling & Statistical Analyses Methods

Data entry

Image data were double entered into a specially developed dataset (EpiData Entry v 2.1) at both baseline and follow up. Consistency checks were performed each evening and inconsistencies corrected the same day.

Data analysis

The International Society for Geographical & Epidemiological Ophthalmology (ISGEO) categorises glaucoma in to Primary Open Angle Glaucoma (POAG) and Primary Angle Closure (PAC) based on direct viewing of the angle. POAG is defined in three categories based on the optic nerve VCDR, visual fields, IOP, VA and the presence or absence of previous glaucoma surgery (clinically or from medical records). [22] The mean, 97.5th and 99.5th percentiles were calculated for optic disc VCDR and IOP for the participants at follow-up. Based on baseline normative data the cut off points required for ISGEO POAG classifications were used to classify accordingly: [22]

- **Category 1 with structural and functional evidence**: Eyes with a VCDR or VCDR asymmetry ≥97.5% for the normal population that showed a definite visual field defect consistent with glaucoma

- **Category 2 (advanced structural damage with unproven field loss):** Eyes of those without any or with no valid visual field testing but with a VCDR or asymmetry ≥99.5th percentile for the normal population.
- **Category 3 (no view of optic disc and field testing impossible):** Eyes of those with VA<3/60 and the IOP>99.5th percentile, or VA<3/60 and evidence of glaucoma filtering surgery, or previous diagnosis of glaucoma confirmed from medical records.

Glaucoma suspects were defined as:

- *field suspects*: those with abnormal visual fields consistent with glaucomatous changes but no raised IOP, disc damage or features consistent with trabecular obstruction,
- *disc suspects*: those with VCDR ≥97.5th percentile for the population but less than the 99.5th percentile and no other feature of glaucoma and no documented field defect. It also included those with optic disc hemorrhages accompanied by no other feature of glaucoma
- *Ocular Hypertensives:* IOP ≥97.5th percentile with normal optic disc and normal visual field

A normative sample was used to calculate the 97.5th and 99.5th percentiles of VCDR and IOP from those participants examined at follow-up with normal visual fields.

<u>Baseline to follow-up changes</u>

It was not possible to produce an annual glaucoma incidence due to the lack of reliable visual field data and optic discs graded from images at baseline and therefore

it was not possible to define an "at-risk" baseline group. Individuals at follow-up were classified as suspect or definite glaucoma based on ISGEO criteria using graded images of the optic disc and visual fields. Participants at follow up were then classified in a binary manner as normal or glaucoma (glaucoma if ISGEO categories 1, 2 or 3 were fulfilled for that participant). Multivariable logistic regression analyses were conducted to compare those with and without features of glaucoma at follow-up in terms of baseline demographic, anthropometric and ocular features as potential risk factors of glaucoma.

Results

Follow up rates

At baseline, 4,414 participants had a complete assessment and 2,171 participants were seen at follow up. Characteristics of participants and non-participants at six-year follow-up are described in detail elsewhere.[23, 24] In summary, compared with those followed-up, participants who had died during follow-up were older, more likely to be male, to have lower education levels and higher systolic blood pressure and be diabetic, but had lower BMI. Compared with participants seen, those lost to follow-up (not known to be deceased) were less likely to be Kikuyu or Kalenjin speakers, had lower levels of education, and were more likely to be from urban areas and be from either the highest or lowest socioeconomic quartile.

Anterior Chamber OCT

Anterior segment findings at baseline using OCT are described in Table 1, the mean angle opening distance (n=6,259) was 631µm (SD:167), the mean anterior chamber angle (n=3,484) was 36.6° (SD:7.6), the mean central corneal thickness (n=6,365) was 508.1 µm (SD:36.9), and the mean anterior chamber depth (n=6,358) was 2.67mm (SD:0.32)

Table 1. OCT Summary of normative findings of the anterior segment at baseline

	Right Eye	**Left Eye**	**Both eyes**
N	3115	3144	6259
Mean Angle Opening Distance (µm) (SD)	620(164.5)	637(179.5)	631(167.3)
N	1774	1807	3484
Mean Anterior Chamber Angle (SD)	36.3(7.7)	37.0(7.5)	36.6(7.6)
N	3179	3186	6365
Central Corneal Thickness (µm) (SD)	507.7(35.7)	508.5(38.1)	508.1(36.9)
N	3177	3181	6358
Anterior Chamber Depth (mm) (SD)	2.66(0.32)	2.68(0.32)	2.67(0.32)

Gonioscopy

Anterior Segment OCT was not available at follow-up, however 2,111 right eyes and 2,107 left eyes had a direct visualisation of the angle using a 4-mirror gonioscope, with only five right and five left eyes (0.2%) considered to have occludable angles (based on visualisation of Schwalbe's line and the anterior meshwork or less). Table 2.

Table 2. Gonioscopic grading of the angle in the follow-up of the Nakuru Eye Disease Cohort Study

Gonioscopic visualisation (Grade)	Right Eye	Left Eye
Nil (0)	0 (0%)	2 (0.1%)
Schwalbe's line and anterior meshwork (1)	5 (0.2%)	3 (0.1%)
Posterior pigmented meshwork (2)	90 (4.3%)	98 (4.7%)
Scleral Spur (3)	797 (37.8%)	809 (38.4%)
Ciliary Band (4)	1219 (57.8%)	1195 (56.7%)

Intraocular Pressure

The mean IOP at baseline based on 3,745 observations (right eye only) was 15.3mmHg (SD 3.4, Range 2-46mmHg). Of these, there were 1,775 observations (right eyes only) for whom IOP was measured at both baseline and follow-up. Among these, at baseline mean IOP was 15.4 (SD 3.4) for the right eye, and at follow-up (right eyes) was 15.0mmHg (SD 3.2, Range = 1-34mmHg), providing evidence of a lower IOP at follow up compared to baseline among right eyes ($p<0.001$). IOP was significantly higher in the right eye than the left eye at both baseline ($p<0.001$) and follow-up ($p=0.02$). See Table 3

Table 3. Intraocular Pressure in the Nakuru Eye Disease Cohort

	Baseline (whole sample)		**Baseline who were followed up**		**Follow up**	
	Right Eye (n=3,745)	Left Eye (n=3,746)	Right Eye (n=1,784)	Left Eye (n=1,776)	Right Eye (n=1,784)	Left Eye (n=1,776)
Mean pressure (mmHg)	15.3	14.5	15.4	14.6	15.0	14.9
Sample Standard Deviation	3.4	3.0	3.4	2.9	3.3	3.2
Confidence Interval for Estimate	15.2-15.4	14.4-14.6	15.2-15.6	14.5-14.7	14.9-15.2	14.7-15.0
97.5th Percentile (95% CI)	22.0 (20.0-22.0)	20.0 (20.0-20.0)	22.0 (20.0-23.0)	20.0 (20.0-20.0)	22.0 (21.0-23.0)	21.0 (21.0-22.0)
99.5th Percentile (95% CI)	28.0 (27.0-28.0)	24.0 (23.5-28.0)	28.0 (25.3 - 29.9)	25.1 (22.3-27.9)	27.1 (25.0-28.9)	26.0 (24.0-28.9)

Optic discs

At baseline, due to camera failure preventing image acquisition in one third of clusters, a slit lamp based clinical assessment of the optic disc vertical cup to disc ratio (VCDR) was made in two ways:

1. Through undilated pupils with +90D lenses using slit lamp biomicroscopy (n=5,917 eyes)
2. After dilating pupils with +90D lenses using slit lamp biomicroscopy (n=7,821 eyes)

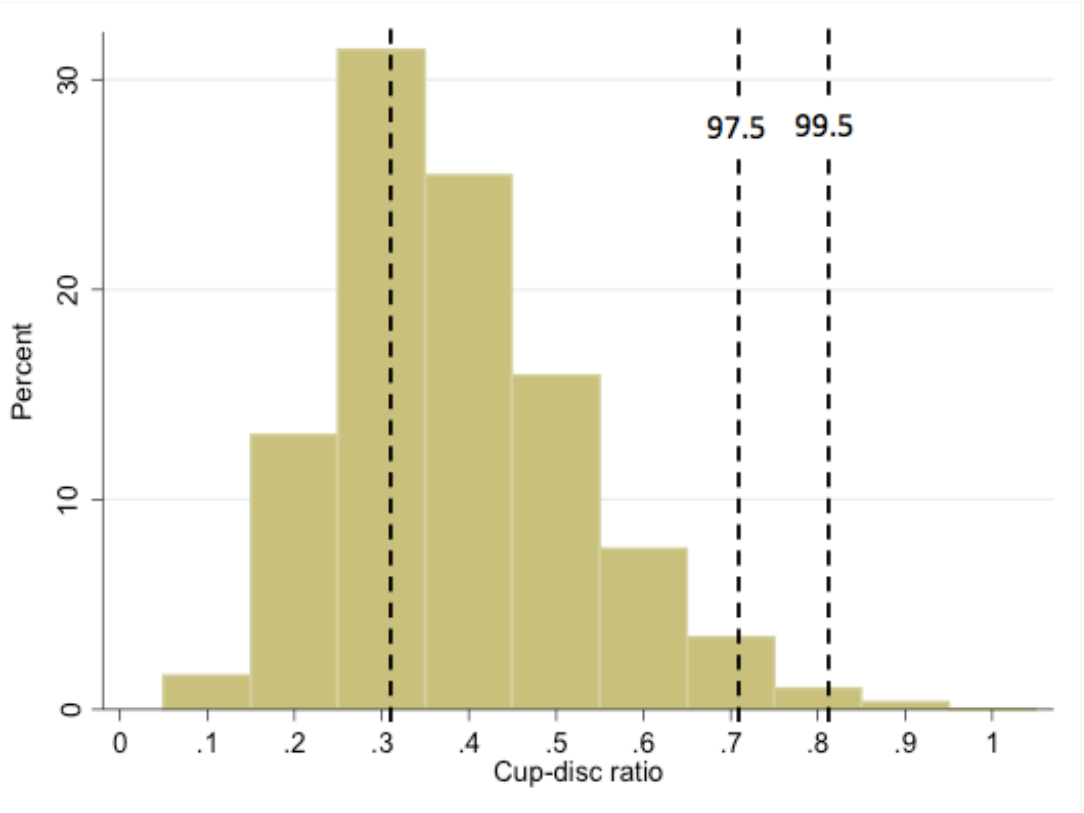
Baseline optic disc assessment is summarised in Table 4.1,063 (25.7%) Right Eye discs and 1,078 (25.8%) Left Eye Discs could not be visualised with undilated pupils. There was a statistically significant difference between the mean VCDR for eyes with pupils dilated and non dilated pupils where the disc was visible in both instances, with the dilated eyes having higher VCDR ratios (0.23, SD 0.15) than non dilated eyes (0.21, SD 0.13) (paired t test<0.001). Using undilated CDR 1.5% of eyes had CDR≥0.7 while using dilated CDR, 2.8% of eyes had VCDR≥0.7 (X^2=13.8 p=0.002).

Table 4. Baseline clinical (undilated and dilated) optic disc assessment made at the slit lamp

	Undilated assessment			Dilated assessment		
	Right VCDR (95%CI)	**Left VCDR (95%CI)**	**Right and Left (95%CI)**	**Right VCDR (95%CI)**	**Left VCDR (95%CI)**	**Right and Left (95%CI)**
Number	2958	2959	5917	3906	3915	7821
0.5th Percentile	0.1(0.1-0.1)	0.1(0.1-0.1)	0.1(0.1-0.1)	0.1(0.1-0.1)	0.1(0.1-0.1)	0.1(0.1-0.1)
2.5th Percentile	0.1(0.1-0.1)	0.1(0.1-0.1)	0.1(0.1-0.1)	0.1(0.1-0.1)	0.1(0.1-0.1)	0.1(0.1-0.1)
Mean(SD)	0.21 (0.14)	0.22 (0.13)	0.21(0.13)	0.23 (0.16)	0.23 (0.15)	0.23(0.15)
97.5th Percentile	0.6(0.5-0.6)	0.6(0.5-0.6)	0.6(0.5-0.6)	0.7(0.6-0.7)	0.6(0.6-0.7)	0.7(0.6-0.7)
99.5th Percentile	0.8(0.8-0.9)	0.8 (0.7-0.9)	0.8(0.8-0.8)	0.9(0.8-1.0)	0.84(0.8-0.9)	0.9(0.8-0.9)

At follow up, the VCDR for right and left eyes from image grading were available in all clusters from 3,658 of a possible 4,342 eyes (2,171 people). The median VCDR was 0.3 and at the 97.5th and 99.5th percentile it was 0.7 and 0.8 respectively. See Figure 1.

Figure 1. The distribution of VCDRs at follow up from retinal images



The VCDR percentiles at follow-up in those with a normal visual field (n=1062) remained at 0.7 and 0.8 at the 97.5th and 99.5th percentiles respectively.

At baseline, 3,251 participants had a clinical assessment (i.e. no image grading) of the optic discs, of which 40 (1.2%) were considered abnormal, 536 (16.5%) suspicious and 2,675 (82.3%) normal. At follow-up, 2,003 participants had an image-based assessment of the optic discs, of which 64 (3.2%) were graded as abnormal, 234 (11.7%) suspicious and 1,705 (85.1%) were normal. 89 of 1,255 (7.1%) participants who had a baseline (clinical) and follow-up (image) assessment went from "normal" to either "suspicious" or "abnormal". Of the 1,499 participants who had optic discs graded at both baseline (clinical) and follow-up (image)171 (1.1%) were considered abnormal, 236 (15.7%) suspicious and 1246 (83.1%) as normal at baseline. At follow up there were 53 (3.5%) considered abnormal, 174 (11.6%) suspicious and 1272 (84.9%) normal.

Visual Fields

Interpretation based on visual fields was not possible at baseline. A total of 508 participants (glaucoma suspects and non-glaucoma suspects) were indicated for visual field testing at baseline of whom 342 (67.3%) completed the test on the Humphrey Visual Field Analyser. Of these, 63.2% and 69.1% of normal and glaucoma suspects had abnormal visual field results despite good reliability indices. These baseline results were therefore discarded.

At follow-up, 1,309 (60.3%) participants successfully completed fields on the Henson 8000 Field Analyser with reliable results. 1,074 (82.0%) were normal in both eyes, 122 (9.3%) had one or both eyes with suspicious fields and 113 (8.6%) had an abnormal field in one or both eyes.

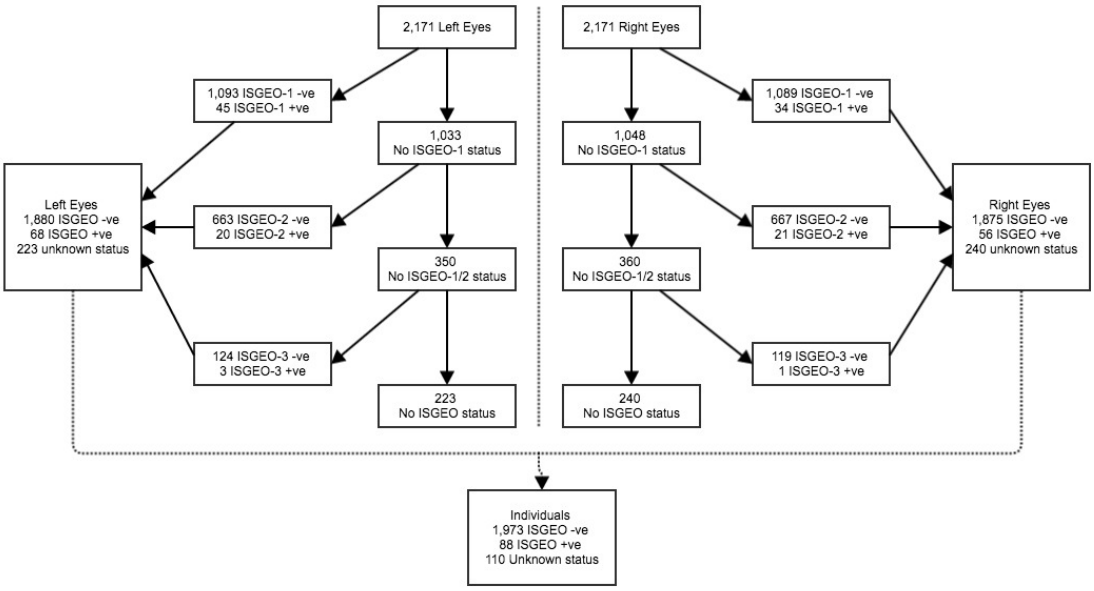
Based on gradable optic disc images at follow-up in those with normal visual fields, the 97.5th and 99.5th percentile VCDRs were 0.7 and 0.8 respectively (Fig 1).

Signs of glaucoma

At follow-up, 1,246 individuals had a VF measurement and a disc grading. Of these, 895 (71.8%) had both a normal VF and a normal disc, 141 (11.3%) had a normal VF and suspicious or abnormal disc, 182 (14.6%) had a suspicious or abnormal VF and normal discs and 28 (2.2%) had both suspicious or abnormal VFs and suspicious or abnormal discs.

Using the ISGEO classification 88 participants were considered to have glaucoma based on meeting either the ISGEO 1 (n= 64), 2 (n=22) or 3 (n=2) criteria, 1,973 participants did not meet ISGEO criteria and were deemed non-glaucoma, 110 could not be classified. (Figure 2)

Figure 2. The ISGEO Classification of the Nakuru Eye Disease Cohort follow-up group



No ISGEO status due to missing data

Based on follow up optic disc grading from images, visual fields, IOP and visual acuity, participants were defined as glaucoma positive or negative based on the ISGEO criteria. Vision status comparing participants with and without ISGEO glaucoma are described in Table 5 showing participants with glaucoma were more likely to have visual impairment. 85.2% of the non-glaucoma group classified as normal vision, compared to 72.7% in the glaucoma group. Blindness and VI were more prevalent in the glaucoma group, 5.7% and 21.6% respectively compared to those without glaucoma, 1.2% and 13.6% respectively.

Table 5 . Visual status of participants at follow-up with and without glaucoma

ISGEO	**Normal vision (≥6/12) [%]**	**Visually impaired (<6/12-3/60) [%]**	**Blind (<3/60) [%]**
Negative (N=1972)	1680 [85.2]	269 [13.6]	23 [1.2]
Positive (N=88)	64 [72.7]	19 [21.6]	5 [5.7]

Baseline and follow-up risk analyses was conducted and is summarised in Table 6. Associations with glaucoma was evident for several baseline factors.

Moderate association was found with participants being more likely to be categorised with glaucoma if they were of male gender (Male as baseline, Female OR: 0.69, 0.45-1.06, p=0.097).

No association was found between baseline IOP and BMI (p=0.49), height (p=0.58) and weight (p=0.28). Associations with ophthalmic signs at follow up were seen for both IOP (IOP>21mmHG OR: 4.10 (95%CI, 2.08-8.08), p<0.001) and a relative afferent pupillary defect (RAPD) showing a particularly strong association with being categorised as glaucoma (Confirmed RAPD OR: 7.39 (4.20-13.01), p<0.001).

Table 6.Association of anthropometric risk factors at baseline and ophthalmic risk factors at follow-up with glaucoma at follow-up

	Category	N total	Abnormal	Percentage	Odds Ratio	Lower 95% CI limit	Upper 95% CI limit	p-value
Gender	Male	989	50	5.1%	1.00			
	Female	1072	38	3.5%	0.69	0.45	1.06	0.10
Location	Rural	1559	60	3.8%	1.00			
	Urban	502	28	5.6%	1.48	0.93	2.34	0.13
Socio Economic Status	Poorest	464	23	5.0%	1.00			
	Poorer	574	20	3.5%	0.69	0.38	1.28	
	Richer	532	27	5.1%	1.03	0.58	1.81	
	Richest	480	17	3.5%	0.70	0.37	1.34	0.53
Tribe	Kikuyu	1336	58	4.3%	1.00			
	Kalenjin	507	16	3.2%	0.72	0.41	1.26	
	Other	218	14	6.4%	1.51	0.83	2.76	0.19
BMI Category	Underweight	195	9	4.6%	1.00			
	Normal	913	36	3.9%	0.85	0.40	1.79	
	Overweight	540	27	5.0%	1.09	0.50	2.36	
	Obese	340	12	3.5%	0.76	0.31	1.83	0.69
Hypertensive	No	1250	54	4.3%	1.00			
	Yes	799	33	4.1%	0.95	0.61	1.49	0.84
Diabetic	No	1839	77	4.2%	1.00			
	Yes	221	11	5.0%	1.20	0.63	2.29	0.58
Education level reported	None	186	6	3.2%	1.00			
	Primary	624	26	4.2%	1.30	0.53	3.22	
	Secondary	1034	50	4.8%	1.52	0.64	3.61	
	College/Uni	215	6	2.8%	0.86	0.27	2.72	0.49
CCT	<=550	1484	55	3.71%	1.00			0.44
	>550	160	4	2.50%	0.67	0.24	1.86	
RAPD*	No	1,831	57	3.11%	1.00			
	Yes	99	19	19.19%	7.39	4.20	13.01	<0.001
IOP*	<=21	1,920	75	3.91%	1.00			
	>21	77	11	14.29%	4.10	2.08	8.08	<0.001
Gonioscopy*	Open	2040	87	4.26%	1.00			0.28
	Occludable	8	1	12.50%	3.21	0.39	26.35	

* Follow-up risk factor

Discussion

In this study we have described the population distributions and normative ranges from an epidemiological survey of glaucoma in an East African population in Kenya. Structural damage manifest by optic nerve changes was comparable in terms of the population distribution to other studies (described below). In those with glaucoma at follow-up, the strongest predictors were the presence at follow-up of an RAPD and IOP above 21mmHg. No demographic or anthropometric risk factors were associated with glaucoma.

The prevalence of glaucoma on those followed up was 4.3% (CI, 3.5-5.9) which is comparable to other population based studies in Africa which range from 4.2% (3.5-4.9) to 7.3% (5.5-9.1)[25, 26] with a higher prevalence in west African populations (Nigeria 5.0% (4.6-5.5) and 7.3% (5.5-9.1),[26] Ghana 6.5% (5.8-7.1)[27]) than is East and Southern African populations (Tanzania 4.2% (3.5-4.9),[25] South Africa 4.5% (3.2-6.1)[28] and 5.3% (3.9-7.1)[29]).

The basis of the diagnosis of glaucoma in the majority of cases, both in clinical settings and in population based surveys, is correlation of structural optic nerve damage and loss of function demonstrated by visual field testing.[30] However, in SSA, where equipment constraints are considerable,[31] visual field testing is not widely available. A survey in Lagos State, Nigeria identified one visual field analyser for every 2,380,000 population including private and governmental facilities. [32] Even where field analysers are available, they are of much less importance in the diagnosis and treatment decision making process than in more resource intense settings; visual field changes were a factor in only 4% of treatment decisions in a review of 344 patients attending a glaucoma clinic in South African.[33] There is an

additional problem due to lack of availability; Population based studies have demonstrated that there are substantial difficulties in achieving adequate field testing in SSA populations. [34]

The lack of a reliable visual field in the baseline of this cohort is consistent with other studies in the region that have faced similar challenges such as the Nigerian National Blindness Survey that used a relatively simple testing modality, the Humphrey Frequency Doubling Technology test, where adequate testing was only available for 60% of 4,538 Nigerian patients.[34] Furthermore, the logistical problems obtaining reliable visual field tests mean that they were not included in the flow chart for community diagnosis of glaucoma in a recently published West African algorithm; relative afferent pupillary defect testing was the chosen test of nerve function,[35] which the findings of this study concur with.

Diagnosis and management of glaucoma in SSA, therefore, centres very much around IOP and optic nerve assessment, the latter through direct visualisation and pupil assessment. Very little data from longitudinal population-based cohorts exist, with none to date from SSA, on glaucoma. This cohort study of people aged 50+ undertaken in Nakuru, Kenya, with baseline in 2007-8 and follow-up in 2013-14 was an opportunity to estimate the normative range of various features of glaucoma as well as potential features that are important for clinical decision making in a context where availability of equipment is limited.

The percentile distributions of optic nerve VCDR and IOP in the Nakuru Cohort follow-up subgroup in whom image grading was available was very similar to the Nigeria National Blindness survey, a nationally representative survey of adults 40

years and older, which is to our knowledge the only National survey in SSA to derive percentile values for defining glaucoma in population-based surveys. [36]. At the 97.5th and 99.5th percentiles the VCDR in Kenya was 0.7 and 0.8 respectively and 0.75 and 0.95 in Nigeria (in all the population with gradable disc images). The median VCDR was lower in Kenya at 0.23 compared to 0.4 in Nigeria. [36]. Our findings are also consistent with other population-based studies in the region where a VCDR of 0.7 was consistent at the 97.5th percentile however greater variation is found at the 99.5th from 0.7 in Tanzania to 0.9 in South Africa. [27, 29, 37, 38]

The IOP distribution in Kenya was similar at baseline and follow-up with a higher median than in Nigeria (15 vs. 14mmHg) but lower IOP at the 97.5th and 99.5th percentiles (Kenya: 22, 27mmHg vs. Nigeria: 24, 34mmHg).[36]

Changes over the period of the cohort were difficult to define conclusively due to the clinical nature of a glaucoma diagnosis, however a strong association between optic discs and visual fields considered to be outside of normal range was demonstrated, in particular with the relative afferent pupil defect (RAPD) test. An IOP over 21mmHg was also less strongly associated with glaucoma as defined by the ISGEO criteria in this study. The findings suggest a combination of optic nerve assessment by both visualisation including VCDR grading as well assessing function through the RAPD test are practical means for identifying individuals who have or are at risk of sight loss from glaucoma. Portable tools for assessing vision [39] and optic disc imaging [40] may make this more accessible with IOP being a suitable method to monitor an effect from treatment and various handheld tools now available for accurate IOP assessment independent of a slit lamp.

Management of glaucoma remains a major challenge in SSA with limited availability and poor adherence to medical treatment when available. A primary surgical approach has problems also, in that patients presenting due to visual loss in one eye need to be persuaded to undergo surgery, most frequently with direct financial costs to them, in the other eye which they do not as yet consider to have a problem. [11, 41] The operation of choice, trabeculectomy augmented by anti-metabolites, does not improve the vision in most cases, but in fact can lead to visual acuity reduction. Identification of new treatment options in Africa therefore remains a priority.

Strengths of this study included it being a large, population-based sample, representative of a population on which there is minimal data. A senior ophthalmologist examined all study participants at baseline and follow up. High quality, modern, equipment was used throughout.

Limitations included a high loss to follow up (50%) at six years, this was primarily due to post-election violence affecting the study population with large numbers of people displaced or killed. Major variations in baseline and follow-up data collection protocols were employed, in part due to challenges at baseline such as unreliable visual field data, retinal camera break down and due to a lack of availability of all baseline equipment at follow-up, e.g. no repeat AC-OCT was undertaken. Key measurement differences and therefore potential measurement bias were in the following tests: i) optic nerve grading at baseline was primarily based on clinical assessment at the slit-lamp with only a minority having image grading, optic nerve grading at follow-up was based on images only, ii) visual fields at baseline were completed for glaucoma suspects (n=165) and a sub-set of normal participants

(n=343) (11.6% of all baseline participants) using a Humphrey field analyser with outputs that could not be confidently used to make an assessment of glaucoma, the Henson 8000 was used at follow-up, iii) anterior chamber angle assessment at baseline was based on AC-OCT and on 4-mirror gonioscopy at follow-up, iv) a statistically significant variation between right and left eye IOP at baseline and follow up. IOP was on average higher in the right than the left eye at both baseline and follow-up. This may have arisen because the right eye was tested first and/or because the majority of the population was assumed to be right-handed, and IOP measurement is associated with hand dominance. [42, 43]

In conclusion, glaucoma remains a public health concern. However, the lack of cost-effective treatments and challenges identifying high-risk individuals means that population-based screening for open-angle glaucoma should not currently be recommended. [44] Further research in to the risk factors, natural history and aetiology of glaucoma in Africa and the barriers to effective sight loss prevention are required.

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Chapter 11. Six-Year Incidence of Visually Impairing Cataracts in Kenya. *The Nakuru Eye Disease Cohort Study*

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Student	Andrew Bastawrous
Principal Supervisor	Hannah Kuper
Thesis Title	The Nakuru Eye Disease Cohort Study

If the Research Paper has previously been published please complete Section B, if not please move to Section C

SECTION B – Paper already published

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For multi-authored work, give full details of your role in the research included in the paper and in the preparation of the paper. (Attach a further sheet if necessary)	Study design, data collection, analysis, write up, review, overall lead.

Student Signature: _____ **Date:** 12, April 2017

Supervisor Signature: _____ **Date:** 12, April 2017

Six-Year Incidence of Visually Impairing Cataracts in Kenya.
The Nakuru Eye Disease Cohort Study

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Abstract

Objective: To provide six-year cumulative incidence of visually impairing cataract in an older age Kenyan population

Design: Population based cohort study with six-year follow-up (n=2,171; 50% participation)

Main outcome measures: Six-year cumulative incidence of visually impairing cataract, risk factors for incidence, population estimates and required cataract surgical rates to manage incident visually impairing cataract.

Results: The six-year cumulative incidence of visually significant cataract in either eye was 251.9 per 1000 (95%CI: 228.5 – 276.8) with an increase with age from 128.9 per 1000 (107.9-153.2), to 624.5 per 1000 (493.1-739.9) in the 50-59 years and 80 years and over groups respectively. This equates to an annual incidence of visually significant cataract of 45.0 per 1000 people over 50 years. Multivariable analysis showed alcohol consumption, diabetes, education level and increasing age to be associated with incident visually impairing cataract. Extrapolations to all people aged 50 years and older in Kenya indicate that 148,280 (95%CI: 134,510-162,950) individuals are developing new visually impairing cataract in either eye (<6/18 in worst seeing eye), and 9,540 (6,610-13,750) are becoming cataract blind in both eyes (<3/60 better seeing eye).

This indicates that a cataract surgical rate of 232 operations per million of population is required to match the annual new cases of cataract blind persons and a CSR of 2,000 for unilateral cataract with visual acuity of <6/60. This goes up as the threshold for surgery goes down.

Conclusions: This six-year follow-up of a cohort indicates a high incidence of visually impairing cataract that remains the priority for prevention of blindness programmes in the region.

Introduction

The prevalence and incidence of cataract is known to rise with increasing age, and consequently the magnitude of visually impairing cataract is expected to continue to grow with population ageing and increases in life expectancy.(1) Half of all cases of blindness worldwide are attributed to cataract.(2) Cataract disproportionately affects people living in low and middle-income countries and persons of African descent.(2, 3) Multiple population-based studies have been conducted examining the prevalence of cataract in sub-Saharan Africa (4) with a considerable variation in prevalence across the continent. However, surveys routinely show that cataract is the leading cause of blindness in sub-Saharan Africa, (4) and a leading cause of visual impairment.

Management of cataract involves surgical removal of the lens and insertion of an intraocular lens and is considered one of the most cost-effective health interventions worldwide.(5) Determining the cataract surgical rate needed to control cataract blindness depends on being able to estimate the incidence of cataract. However, the only incidence data on cataract from populations of African descent comes from outside the African continent. The best estimates come from the Barbados Eye Studies in which a nine-year follow up of an adult population, 40 years and over, of African descent were completed, and showed incidence rates of any cortical and any nuclear opacities over nine years were 33.8% and 42.0%, respectively and were higher in participants of African descent than Caucasians (Risk Ratio: 1.8; 95% confidence interval,1.2–2.8), .(6-9) Incidence data are urgently needed for Africa, to ensure appropriate planning and allocation of scarce human resources and equipment.

We aimed to estimate the six-year cumulative incidence of visually impairing and blinding cataract in an East African adult cohort of people 50 years and above in Nakuru, Kenya.

Methods

The methodology of the Nakuru Eye Disease Cohort Study has been reported in detail previously (10), and is summarised here.

Ethical Approval

The study adhered to the tenets of the Declaration of Helsinki and was approved by the Ethics Committee of London School of Hygiene & Tropical Medicine at both baseline and follow-up (LSHTM Ref 6192). Baseline approval was provided by the Kenya Medical Research Institute Ethics Committee and by the African Medical and Research Foundation (AMREF) Ethics Committee, Kenya for the follow-up (AMREF-ESRC P44/12). For both phases approval was granted by the Rift Valley Provincial Medical Officer and the Nakuru District Medical Officer of Health. Approval was sought from the administrative heads in each cluster, usually the village chief. They were also given a copy of the consent form to read and pass on to those in the village.

Informed Consent

The objectives of the survey and the examination process were explained to those

eligible in the local dialect, in the presence of a witness. A subject was examined only after informed written (or thumbprint) consent was obtained. Participants identified with eye conditions, or other health conditions, were referred to local services.

Baseline Study Population

The initial population based survey was conducted in 2007/08. The sample size of 5000 participants aged ≥ 50 years was calculated based on an expected prevalence of VA<6/12 in the better eye due to posterior segment eye diseases (PSED, the primary outcome for the baseline survey) of 3.0% in this age group, precision of 0.5%, design effect of 1.5, and a response rate of 90%.

A total of 100 clusters each of 50 participants were selected with a probability proportional to the size of the population across Nakuru district. Households were selected within clusters using a modified compact segment sampling method (11). An eligible individual was defined as someone aged ≥50 years living in the household for at least three months in the previous year. All participants were invited to undergo a comprehensive ophthalmic examination at a screening clinic (details below).

Follow-up

Follow-up of the cohort was conducted from January 2013 to March 2014.

Retracing at Follow-up - Advance Team

Approximately one week before the follow-up examination clinic was planned for a given cluster, a field officer studied the maps of the village including GPS coordinates

recorded at baseline and made phone contact with the village chief or guide to arrange the visit. At the planning visit, a list of study participants were given to the chief and a local village guide was recruited to assist location of the study participants. At this visit the examination site was established and identification of amenities such as electricity, water and road access were made. Two days prior to the clinic, the field officer reminded chiefs of the visit by phone and notified them and the guide of the advance team's arrival.

On the day prior to the examination clinic, the Advance Team visited homes of baseline participants and confirmed their identity using National Identity cards and invited them to attend the examination clinic the following day. All identified participants were also asked to help locate baseline participants that had not been found.

Examination Clinic (Baseline and Follow-up)

The following procedures were undertaken for all participants who attended the examination clinic at baseline and follow-up and further details are available elsewhere.(10) Further procedures were undertaken that are not included here as they are not relevant to the outcomes being reported (e.g. visual field assessment).

1. ***Registration***

On the examination day, the advance team confirmed the identity of participants against data from baseline (age, date of birth, name, and identity cards). In cases of uncertain identity, confirmation was made based on retinal examination verified by comparison with the baseline photo.

2. *Visual Acuity Assessment*

A clinical officer determined whether the study participant:

a) Was wearing distance correction glasses

b) Owns distance correction glasses but failed to bring them

c) Does not own any distance correction glasses

d) Routinely uses reading glasses

e) Was wearing aphakic glasses

Visual acuity (VA) was measured using a back-illuminated modified LogMAR reduced tumbling E chart (Sussex Vision Inc) (12, 13), which has been used in previous population based studies. (14, 15)

VA was used to define eye and person level (based on the better seeing eye) categories of vision as follows: Normal (≤6/12 Snellen, LogMAR ≤0.3), Mild VI (<6/12-6/18, <0.3-0.48), Moderate VI (<6/18-6/60, <0.48-1.0), Severe VI (<6/60-3/60, <1.0-1.3), Blind (<3/60, <1.3). The term "Visual Impairment (VI)" is used to define all those with a VA <6/18 to "no perception of light" and is therefore inclusive of moderate VI, severe VI and Blind.

3. *Lens Assessment*

Pharmacologic dilation of the subject's pupils was achieved by using tropicamide 1% (Mydriacyl) with phenylephrine hydrochloride 2.5% if needed. The anterior segment was examined by the study ophthalmologist (WM at baseline, AB at follow-up) using

slitlamp biomicroscopy. The WHO simplified system for lens grading was used (16) following standard protocols. The lens was also examined for position, the presence of hypermature (Morgagnian) cataract, and previous lens surgery (aphakic or pseudophakic). A red reflex lens image was taken when each participant was having retinal photographs. Pseudophakic participants were assessed for the presence or absence of posterior capsular opacification and, if present, whether it entered the visual axis.

4. Anthropometry

A nurse performed and recorded measures of participants: height (Leicester Height Measure, Chasmors Ltd, London); weight (Seca 761 Medical Class 4 Scales mechanical ground scale, Williams Medical Supplies, London); waist and hip circumference (Chasmors WM02 Body Tape measure), and three measures of blood pressure (Omron® Digital Automatic Blood Pressure Monitor Model HEM907), each ten minutes apart. In addition, at follow-up, bioimpedence (Tanita Segmental Body Composition Monitor) was performed.

At baseline, capillary blood was taken from all participants for random blood glucose, in addition at follow-up glycosylated haemoglobin was taken in all with a self-reported history of diabetes, or random blood glucose of ≥7.0mmol/L and a further 10% of non-diabetics (based on history and random blood glucose).

5. Interview

An interviewer performed a structured interview in the participant's preferred

language covering i) demographic details including; name, year of birth, ethnicity and education level; ii) past medical and ocular history including medical or ophthalmic medication or surgery and relevant family history; iii) known risk factors, including smoking and tobacco consumption and alcohol intake; iv) socioeconomic status based on job, housing conditions, ownership of material goods and livestock which is translated in to a score based on previous work in the same population.(17)

Definitions and Statistical Analyses

Visually impairing cataract was defined as an individual with vision in the better seeing eye of <6/18 and the presence of a gradable cataract (nuclear, cortical, posterior capsular or mixed using the WHO Simplified Cataract Grading System (16)), mature cataract or hypermature cataract. Definitions of incidence are described in table 1.

All participants who had complete examinations at baseline who were not classified as having a visually impairing cataract were considered to be "at-risk" for incident visually impairing cataract. Follow-up status at 6 years was categorised as i) Found and examined; ii) Found and not examined; iii) Deceased; iv) Moved away; or v) Unknown.

Statistical analysis was performed using STATA v13 (Stata Corp). All analysis accounted for the cluster survey design using Taylor linearized variance estimation to calculate standard errors.

Preparation of cohort for analysis

Pearson Chi-squared tests corrected for the survey-design were used to calculate p-values in order to assess differences between participants seen and those lost to follow-up (LTFU), and between those known to have died and with unknown outcome status.

Those who were deceased and therefore did not have outcome data were then excluded, as they were not eligible for follow-up. Those followed up but without complete records for all covariates at baseline were also removed from the cohort at this stage.

An inverse probability-weighting (IPW) model (18) was then developed, in order to allow estimation of cumulative incidence while accounting for those LTFU. Multivariable logistic regression was used to identify independent baseline covariates associated with LTFU. Covariates for which there was evidence of univariable association with the outcome ($p<0.1$ across all categories of the variable) were kept in a multivariable model, those with $p>0.1$ were excluded from the model. From this final model, the probability of being followed was estimated, based on the presence or absence of each of these baseline covariates. The inverse of this probability formed the weighting to be applied in order to account for those LTFU.

The final step was to remove those individuals LTFU from the cohort, so that all subsequent analysis would be performed on only those with complete outcome records, with IPW applied to account for those LTFU. A sensitivity analyses for this approach involved a complete records analysis (i.e. only including those people who had complete records for outcome and all variables in the analysis).

Estimation of absolute and relative effects

The six-year cumulative incidence of each outcome was calculated by dividing the number of events identified at 6-year follow-up by the number of people at risk at the beginning of follow-up. 95% confidence intervals were estimated assuming a Poisson distribution of events. This was done for the population overall, and stratified by each covariate.

To estimate age-adjusted associations between each outcome (visual impairment and blindness respectively), with baseline covariates, age-adjusted risk ratios for each covariate were estimated using a Poisson regression model with robust error variance to allow for the clustered design and including IPW. For multivariable analysis, an initial model was fitted that included those variables shown to be associated with outcome in age-adjusted analysis (using a Wald test threshold p-value of <0.05 to indicate association). A backward approach was then applied in order to obtain a final multivariable model, removing variables with p>0.05 one-by-one.

Visual Acuity Definitions

WHO definitions of visual impairment and blindness were used throughout (19). Monocular visual impairment is defined as visual acuity <6/18 (20/60) in either eye. Visual impairment is defined as a visual acuity of <6/18 in the better eye. Monocular blindness was defined as a visual acuity of <3/60 (20/400) in either eye. A person was considered to be blind if the visual acuity in the better eye was <3/60. The definition of visual impairment also includes those who were blind.

Diabetes Definition

Diabetes was defined as (1) Self-reported in the history, or (2) random glucose of ≥11.0mmol/L, or (3) HbA1c ≥7.0.

Extrapolation of data

Estimates of cumulative incidence were extrapolated to estimate the number of adults over the age of 50 with incident visual impairment or blindness in Kenya. This was calculated by taking 2015 population estimate from Kenya (Census Bureau of Kenya) by age category and gender and multiplying this by the age and gender specific estimates of annual cumulative incidence.

Cataract Surgical Rate

The estimated number of cataract operations per million of population (all ages) was estimated at different thresholds for surgery based on three levels of vision (blind, severely VI, moderate VI) and whether for person or individual eye. To give an estimated annual cataract surgical rate per million of population.: the annual incidence rate for all ages 50 and above was multiplied by 1,000 and by the proportion of the population who are aged 50 years and above in Kenya (4.3M of 45M in 2015), The CSR calculation assumes there are no cases of blinding or visually impairing cataract in people aged under 50 years, and is therefore likely to underestimate the true incidence by a small amount.

Results

Baseline estimates of prevalence

4,414 participants were recruited at baseline in 2007-2008. 4,364 (98.9%) of these had an examination of the lens and given a lens status.

Out of the 4,364 individuals who had complete eye examinations, 669 had VA<6/12 in the better seeing eye. Of these, 180 subjects were visually impaired (<6/18) from cataract with 32 of them blind, 11 with severe VI (SVI) and 137 with moderate VI. Cataract was the commonest cause of blindness and SVI, being responsible for 45.1% and 61.1%, respectively. 3,591 (82.3%) participants did not have visual impairment or visually significant cataract, i.e. they either had no cataract and vision of 6/18 or better, the presence of cataract but vision 6/18 or better, or vision at worse than 6/18 but no evidence of cataract (Table 1).

The types of lens opacities associated with the level of visual impairment were examined, table 2, with the most common finding being mixed followed by nuclear only, cortical only and posterior subcapsular (PSC) only in all vision categories.

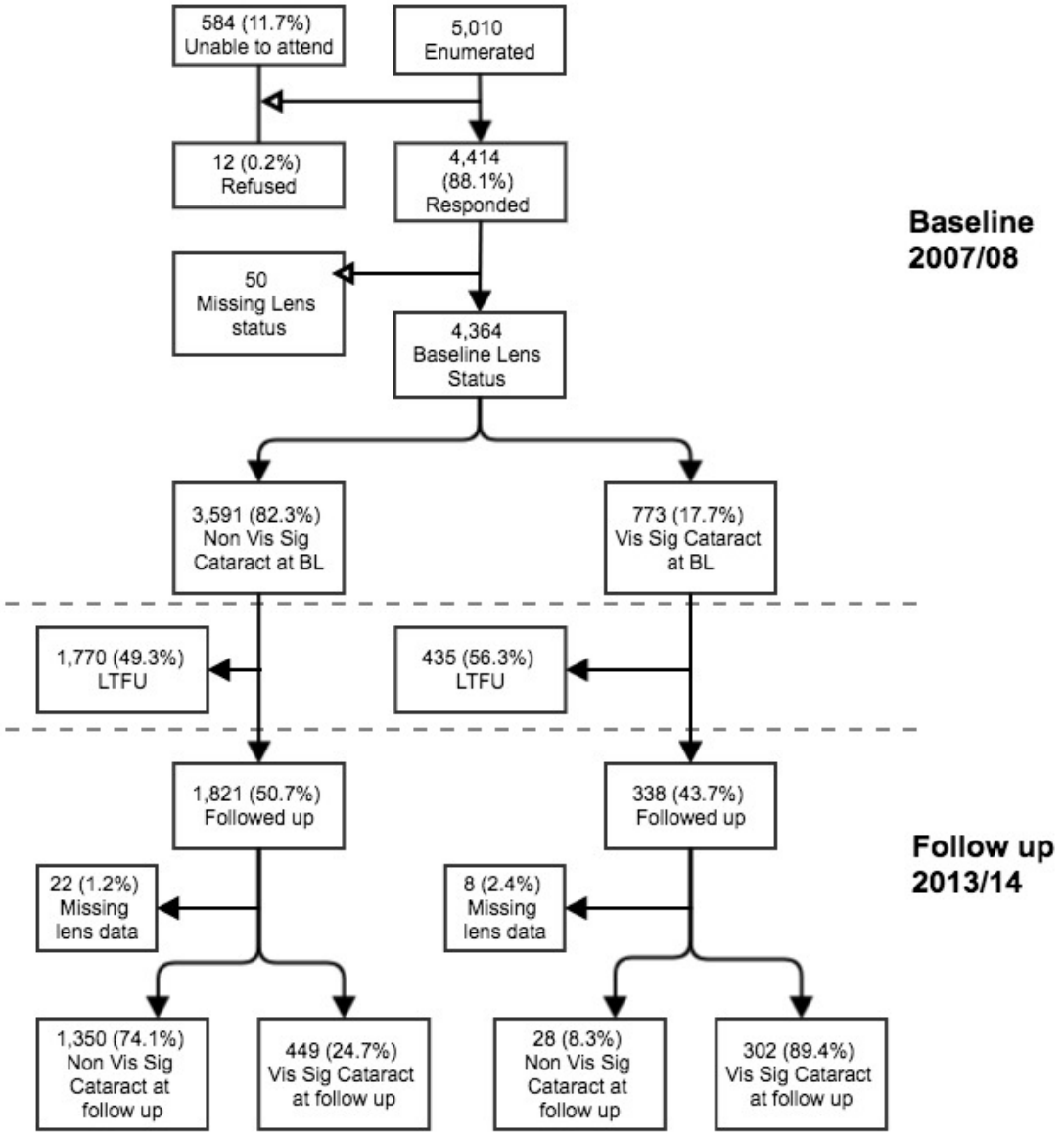
Estimates of incidence

A total of 2,159 (49.5%) participants were followed up in 2013-2014 of whom 2,129 (98.6%) had a complete examination including lens status.

At baseline there were 3,591 participants without visually significant cataract and, 1,821 (50.7%) were followed up with 1,799 (98.8%) having a complete lens examination. Therefore 1,799 participants were at-risk of incident visually impairing cataract of whom 449 (24.7%) in the six-year follow-up period developed a visually significant cataract (the participant newly developed VA of worse than 6/18 with the presence of a cataract), and seven of these had become cataract blind.

1,944 study participants had a cataract on clinical examination at baseline, of whom 773 had a visually significant cataract at baseline with proportionally fewer available for follow up examination (n=330, 42.7%). The majority, 302 individuals (91.5%), of this group had a visually significant cataract at follow-up, while 28 (8.5%) no longer had a visually significant cataract at follow up despite not reporting having had surgery (figure 1). 18 of 284 (6%) individuals at baseline who were referred for cataract surgery had undergone surgery at follow-up.

Figure1. Study participants and visually significant cataract (<6/18 Snellen)



LTFU: Loss to follow up, Vis Sig Cataract: Visually Significant Cataract [VA <6/18 and proven cataract], BL: Baseline

Due to the high loss to follow up (50.5%) a comparison of baseline features between participants who were followed up and those who were not was undertaken (Table 3). There were notable differences between those followed-up and those who were not (and not known to be deceased) (n=1,524, 42.4%), these were: tribal group

[proportionally less Kikuyus and Kalenjins, the two major tribes in those not followed up] and residence [proportionally more rural than urban dwellers followed up]. Notable differences between those followed up and those known to have been deceased included [followed up vs. deceased]: younger mean age [60.9 vs. 67.1years], lower systolic blood pressure [139.1mmHg vs. 145.1mmHg], lower random blood sugar [5.2mmol/L vs. 5.6mmol/L], higher body mass index [10.4% vs. 23.4% underweight at baseline] and lower alcohol consumption.

The six-year cumulative incidence of visually significant cataract in either eye after adjusting for LTFU using the IPW model, was 251.9 per 1000 (95%CI: 228.5 – 276.8) with an increase with age from 128.9 per 1000 (107.9-153.2), 290.5 per 1000 (249.6-335.2), 565.3 per 1000 (489.3-638.3) to 624.5 per 1000 (493.1-739.9) with each decade of life, 50-59 years, 60-69 years, 70-79 years and 80 years and over respectively. (Table 4). This equates to an annual incidence of visually significant cataract of 45.0 per 1000 people over 50 years.

The six-year incidence of persons (better seeing eye) becoming cataract visually impaired, severely visually impaired or blind from cataract was: 134.9 per 1000 (95%CI: 117.1-154.9), 66.6 per 1000 (54.9-80.6) and 13.6 per 1000 (9.4-19.5) respectively. Table 4.

When the cumulative incidence is extrapolated to all people aged 50 years and older in Kenya, the estimated number of individuals developing new visually impairing cataract in either eye, becoming cataract visually impaired (better seeing eye), severely visually impairing cataract in either eye, becoming cataract severely visually impaired (better seeing eye), new cataract blind in either eye and cataract blind (better seeing eye) per year is: 148,280 (95%CI: 134,510-162,950); 86,690 (75,240-99,570); 88,630 (78,140-100,280); 46,690 (38,500-56,480); 44,260 (36,700-53,240) and; 9,540 (6610-13750) respectively (Table 5).

This indicates that a cataract surgical rate of 232 is required to match the annual new cases of cataract blind persons. This goes up as the threshold for surgery goes down, Table 6 and Figure 2.

Figure 2a. Estimated minimal cataract surgical rate (CSR) needed to meet the current annual incidence of visually impairing cataract at different operating thresholds (based on presenting acuity in either the better or worse seeing eye). Horizontal text = annual CSR, vertical text = annual number of new cases in Kenya

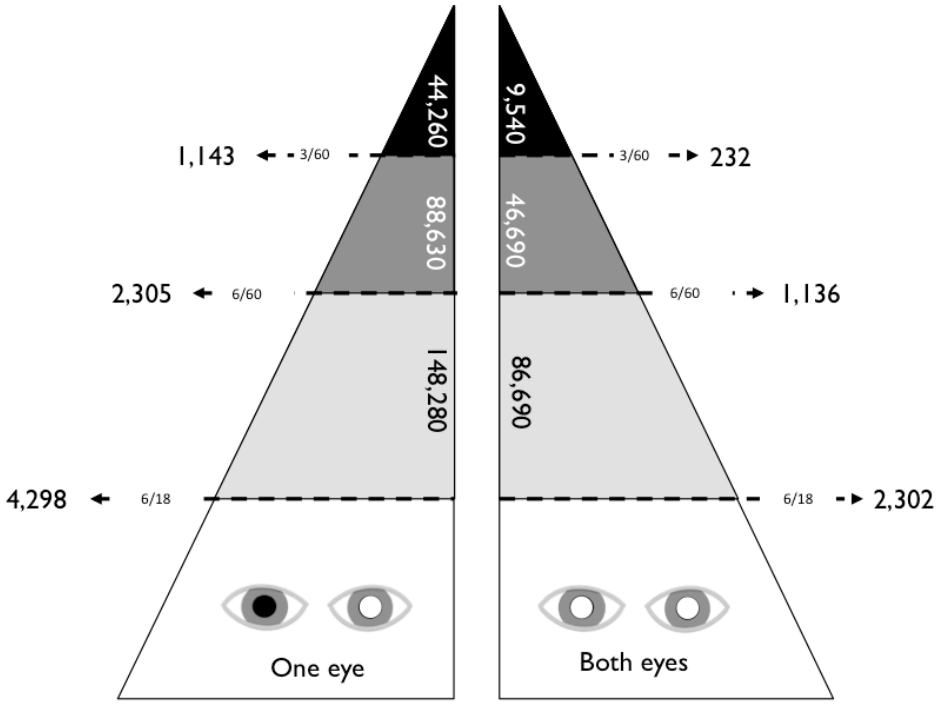
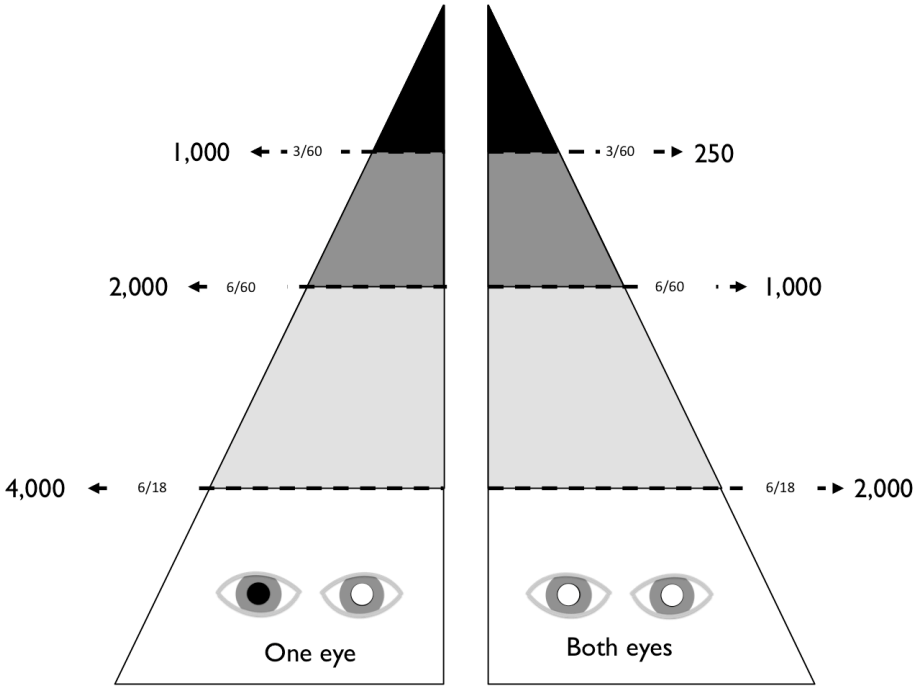


Figure 2b. Simplified CSR pyramid



Multivariable analysis showed alcohol consumption, diabetes, education level and increasing age to be associated with incident visually impairing cataract; With a 1.4 (95%CI: 1.1-1.8) increase risk in current alcohol drinkers vs. never drinkers, former drinkers were not at increased risk; diabetics had a 1.7 (95%CI: 1.3-2.3) fold risk versus non-diabetics; a trend towards less incident cataract with higher education level; and 2.0 (95%CI: 1.6-2.6), 3.7 (95%CI 2.9-4.7), 3.8 (95%CI: 2.6-5.5) increased adjusted relative risks in the 60-69, 70-70 and ≥80 year age categories with 50-59 years as the baseline (table 7).

Discussion

This is, to our knowledge, the first longitudinal population-based study on eye disease in Africa. The annual incidence of visually impairing cataract (<6/18) in either eye in those aged 50 years and over was 45.0 per 1000 people per year and 2.5 per 1000 per year were cataract blind (<3/60 both eyes).

Increasing age, diabetes, alcohol consumption and low education were associated with incident visually impairing cataract. Ageing is a well described risk factor for incident cataract throughout the world. (8, 9, 20, 21) Diabetes is also known to be associated with incident cataract, (22, 23) most cohort studies have not found an association with alcohol consumption however a "u" shaped association was found in an Australian cohort with moderate consumption being seemingly protective compared to abstinence or heavy consumption.(24) There is some evidence of an inverse relationship between education level and incident cataract (25, 26) as demonstrated in this population, notably education level affects incidence of cataract surgery more commonly than cataract formation.(27)

Blindness and VI due to cataract is associated with reduced quality of life (28) and visual function, which can be reversed following low-cost surgical management.(29) Considerable social and economic disadvantages can result from cataract, especially in low-income communities and it contributes to the perpetual cycle of poverty.(30) Conversely, poverty can be alleviated with the provision of cataract surgery.(31) Management of cataract is recognised as a priority of the VISION2020: The Right for Sight global initiative that targets avoidable blindness however, to our knowledge, incidence data including risk factors for incidence of visually impairing cataract has

not previously been available from the African continent limiting the ability to effectively plan and resource services.

Based on a presenting visual acuity of VA <6/18 (Snellen equivalent) in either eye with a cataract verified by dilated slit lamp examination, or the participant being newly pseudophakic, we found the incidence of cataract in this population to be high. As expected, the incidence of visual impairing cataract increased significantly with age. Comparison with other cohorts is limited in part due to a lack of other data from the region and variations on the definition of "visually impairing cataract", however, the estimates from Nakuru show a higher incidence than most other cohort studies outside Africa. (26, 27, 32-34) The high prevalence of untreated cataract in this study may reflect a combination of low access to ophthalmic services and health services in general with the high incidence. (35)

This study also highlighted the low uptake of services in those needing cataract surgery. All participants at baseline identified by the lead ophthalmologist with an operable cataract were offered referral to the regional eye unit. However very few accessed the service with only 18 of 284 (6%) of individuals followed-up after six years having had surgery. Barriers to cataract surgery have been previously described in this population and include: awareness; cost; distance from services; fear and lack of felt need for treatment. (36, 37) Ultimately, these factors mean that visually significant cataract remains untreated.(38)

Strengths of the study include it being a representative population-based sample in an area of ethnic, socioeconomic and educational diversity; a large sample size;

comprehensive assessment of risk factors; high-quality assessment of vision and utilising the same tools at baseline and follow up. The methodology used to assess ophthalmic disease was consistent with studies performed in well-developed health systems in high-income countries such as the USA (39) and Australia (40), with use of the latest available equipment. (10)

The major limitation of this study was low-participation rate at follow-up (50%), however having the baseline characteristics of non-participants is a strength that enabled weighting to ensure better estimates of cumulative incidence. This loss to follow-up may have led to an under or over estimation of incident cataract visual impairment and blindness, depending on the general characteristics of the non-respondents. The predominant risk factor for incident VI or blindness was age and given this was closely matched between participants and non-participants (62.7 years (SD 9.4) and 62.5 years (SD 10.4) respectively) the estimates are likely to be an acceptable reflection. This is further supported by minimal changes being apparent after adjusting estimates for missing data.

Reasons for the low-participation included ethnic violence with displacement of large numbers of people in the study sample area. Post-election violence in 2007 and 2008 led to up to 600,000 people being internally displaced and 1,300 fatalities.(41, 42) In a number of study clusters, entire ethnic groups present at baseline were no longer available or traceable. Great efforts were made to locate individuals on two or three pre-examination visits. We tried to promote attendance by providing transport support and notification of alternative dates to attend clinics in the same locality. Further limitations include restricting the inclusion criteria at baseline to those 50 years and above, reducing the generalizability of our results to the entire population.

This restriction is, however, comparable with the majority of population-based studies of eye disease that restrict inclusion to 40 or 50 years and above. Sampling people aged 50 and above was appropriate for the outcomes of interest given the highest prevalence and incidence is in this age group, making this appropriate both epidemiologically (sample size considerations) and for public health and policy planning purposes.(43) The definition of blindness and visual impairment in this study was based solely on presenting central LogMAR visual acuity and did not include peripheral vision loss. This potentially underestimates the incident visual impairment and blindness when being compared to studies that include these criteria, though this is of less concern with the focus of the paper being on cataract.

Our results suggest that there are 148,280 new cases of eyes with VI (<6/18) due to cataract in people aged 50 years and above per year in Kenya, of whom 9,540 are blind. Extrapolating these estimates suggests that between 232 cataract surgeries (only one eye of people who have less than <3/60 in both eyes); 2305 (all eyes <6/60 with cataract) and 4,298 (all eyes <6/18 with cataract) need to be conducted per million population per year (cataract surgical rate – CSR) to manage the new cataract cases depending on which vision threshold for surgery is used. The current estimate of CSR in Kenya is 550. Recent estimates suggest there are 100 ophthalmologists in Kenya for a population of approximately 45 million, with the majority (50%) being based in the capital city of Nairobi. This leaves 92% of the population (approx. 40 million people) being served by 50 ophthalmologists. Overall Kenya is better resourced than many other African countries in terms of human resources, despite still being well below recommended targets.(44) Continued effort to strengthen the eye health system is necessary to support the growing unmet need of this aging and growing population.

In conclusion, the incidence of visually impairing cataract in this adult, Kenyan population was considerably higher than comparable studies worldwide and remains the priority condition for the prevention of avoidable blindness and visual impairment. High quality, high volume surgery and an increased awareness and demand for services at the community level are required to lower the burden of visual impairment and blindness.

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Chapter 12. Discussion

The aim of this thesis was to estimate the incidence of visual impairment (VI) and blindness, as well as the incidence of the leading visually impairing eye diseases, in an elderly population in Nakuru, Kenya. Overall we demonstrated that this population has a high incidence of visual impairment and blindness, higher than any documented population elsewhere in the world with key differences in disease aetiology to populations in other settings.

The results of this cohort study among older people in Nakuru, Kenya are summarised below

Table. Key finding from the Nakuru Eye Disease Cohort Study

Incidence of	**Incident cases / At risk cases**	**Six year cumulative incidence (N / per 1000 of population, 95% CI)**
Bilateral blindness	29 / 2140	15.1 (10.4 – 21.7)
Bilateral Visual Impairment	234 / 1983	119.4 (103.1 - 137.9)
Unilateral blindness	111 / 1984	54.6 (43.7- 68.0)
Unilateral Visual Impairment	390 /1721	228.0 (206.0 – 251.6)
Diabetes Mellitus	123 / 2056	61.0 (50.3 - 73.7)
Diabetic Retinopathy*	20 / 1421	15.8 (9.5 - 26.2)
Diabetic Retinopathy**	11 / 44	224.7 (116.9 - 388.2)
Age Related Macular Degeneration	202 / 1282	164.2 (136.7 - 195.9)
Visually significant cataract (either eye)	422 / 1799	235.6 (213.5 – 259.3)

*At risk = those without diabetes mellitus or diabetic retinopathy at baseline
**At risk = those with diabetes mellitus and no diabetic retinopathy at baseline

The systematic reviews we conducted on the prevalence of eye diseases in sub-Saharan Africa (SSA) confirmed that there is a wide variation in estimates across the continent and that as a whole, yet overall the prevalence is one of the highest in the world with only Asia having a higher prevalence of visually impairing eye diseases.(1, 2) The per capita human resources to tackle this huge magnitude of disease is lower in SSA than anywhere in the world.(3) Despite Kenya having proportionally more human resources then many of its neighbours, it remains hugely under served and large areas of the country have minimal access to services.

Secondary aims included establishing risk factors for incident VI or blindness and describing the natural history of several eye diseases. We found age and diabetes (independently) to be positively associated with incident VI and blindness. Diabetic Retinopathy (DR) incidence was strongly associated with increasing age, and with higher BMI, urban dwelling and higher socioeconomic status. Incident AMD increased with age as well as independently being higher in persons with diabetes and females. Incident visually impairing cataract was associated with alcohol consumption, diabetes, education level and increasing age. No systemic or anthropometric associations with prevalent glaucoma in the cohort follow up were found, however both a relative afferent pupil defect and high intraocular pressure (>21mmHg) were strongly associated.

The main strengths and limitations of the study have already been discussed in the individual papers. Some key features of the study design are considered here in further detail.

A population-based cohort study in Nakuru, Kenya was chosen for the study. Population-based studies are the most effective designs for establishing reliable estimates of prevalence and incidence and extrapolating that data to the sampled population and other similar populations. Nakuru itself was chosen as it was believed to be relatively representative of Kenya in terms of: the diverse ethnic mix, the mix of rural and urban dwellers, the socioeconomic and educational spread and the age spread of participants. It was also chosen as there had been a previous Rapid Assessment of Avoidable Blindness (RAAB)(4) which showed posterior segment eye diseases to be a leading cause of VI and blindness, as with other studies in the region. Dr Wanjiku Mathenge, who led the RAAB in Nakuru was based in the government hospital in Nakuru and was well placed to lead a comprehensive study of eye disease, which formed the baseline for this cohort.

The large sample size (n = 5,000) at baseline provided accurate estimates (with narrow confidence intervals) for the prevalence of VI, blindness, (5) diabetes, diabetic retinopathy, (6) age related macula degeneration (7) and refractive errors. (8), which were assessed with gold-standard clinical methods, and so provided a strong foundation for a cohort study.

The sampling frame used data from the electoral role (2005) as the most recent census data at the time was from the 1990s. A limitation of this was that estimation

of the proportion of adults aged 50 years and over were taken from the out-dated census resulting in less confidence that the sample probability was proportionate to size although this was not thought to alter the overall findings significantly.

Much of the study design at baseline was repeated at follow-up, which was an important strength. However certain limitations of the baseline study were used to change specific aspects of the follow-up. This included using a difference fundus camera and different visual field analyser. Although the quality of retinal images at baseline was high, the consistency was low with almost one in three clusters having camera failure that meant no images were captured for grading. This considerably reduced the available sample at follow-up for sub-analyses, which required independent image grading at both time points. The visual field analyser used at baseline was found to be unsuitable for this study population. Participants found it difficult to complete with no opportunity for learning or repetition. The test time meant it was only delivered on a 10% sub-set of the sample population and the reliability of these was very low. Despite multiple attempts to assess the raw data from these visual field tests, the entire baseline visual field analysis was reluctantly discarded due to the low confidence in the findings. As a consequence, using the preferred ISGEO classification for glaucoma was not possible and no prevalence data on glaucoma from this baseline sample has been published to date, nor was it possible to estimate the incidence. Another concern with the data at baseline was the use of the WHO definition of diabetes mellitus based on a single random blood sugar of ≥11.1mmol/L. (9) Although this was a suitable choice for this study environment, it incurred limitations around the confidence of a diagnosis from a single, capillary reading done without fasting.

At follow-up, multiple retinal cameras were evaluated which included visiting different manufacturers and discussing the use of these in settings that they are not typically designed for. In the end, the Haag-Streit DRS Centre Vue camera was chosen. This choice was made based on the several key factors: the required power consumption, on-board hard disk for auto-saving and labelling of images, limited moving parts, dust seal and packaged size (suitable for air transport to Kenya and transportation to over 100 sites across Nakuru County). As with the retinal camera, multiple visual field analysers were reviewed, including novel laptop based tests. After discussion with multiple leading experts (thank you to Dr Wormald and Prof Henson), the Henson 8000 was chosen. A final change was made to the baseline protocol in order to further support a diagnosis of diabetes mellitus at follow-up; portable HbA1c kits (Bayer) were used on a sub-set of participants (limited to a sub-set due to cost) as a means of confirming diagnosis in those with a random sugar and evaluating for false negatives.

As expected, the logistical and personal challenges of undertaking such a study were considerable. These ranged from moving to a new country with a young family to having no place to live or team to work with. We had to adapt quickly and prepare carefully. Despite months of preparation there were many things we couldn't prepare for including the national elections that took place mid-way in the study. The tensions leading up to the elections were considerable and many of the clusters we visited had been deeply affected by the post-election violence in 2008. This included entire ethnic groups being untraceable in several clusters, with nobody available to know if they had moved away, died or otherwise. This had a dramatic

effect on the follow-up rate with us only being able to successfully locate 50% of the baseline participants. Huge efforts were undertaken to minimise loss to follow-up. This included several calls to the village chief or senior person in the cluster to explain we were coming and the purpose of our visit. This was followed up by a visit by one of our team members to meet the village chief, gain permission for the study and the allocation of a local guide. The chief and guide would review the list of participants from that cluster marking those they knew and making announcements for the others at local meetings such as church services or farmers markets. A few days later, two of the study's advance team would meet the guide and go together on foot, door-to-door, visiting all the participants known to still be located there. Each confirmed participant was asked to review the list to confirm if they knew others on the list, if they were still alive, where they were or if they were known to have moved away. A clinic site was established on the first visit to ensure all participants were aware of where to come. On the clinic day, the advance team would arrange collection with the team driver of all those who were a considerable distance from the clinic or had limited mobility and/or time. Subsequent clusters were located as close as possible to previous ones to provide a further chance for those who were known to still be alive and located in the cluster to attend a neighbouring cluster had they not been able to make it to their own. Further additional clinics were put on at the end of the study period with all clusters re-contacted and free transport to and from the town based clinics offered.

Despite these efforts, only 50% follow-up was achieved causing potential sampling bias. Comparable studies worldwide (10-24) have had four to six-year follow up rates varying between 53-81% as summarised in the table below. Advice was sought

from several statisticians on how best to handle this loss to follow up including Professor Helen Weiss, Dr Jonathan Bartlett, Dr Kevin Wing and Dr David Macleod at the LSHTM. The model chosen in the end was the "inverse probability weighting" model (IPW), which is detailed in the data papers. Reassuringly, the estimates when using complete case studies and IPW modelling were similar, indicating the lack of important bias in the estimation of incidence. Furthermore, the differences between those followed-up and those who were not were described in detail for each paper.

Table. Comparable cohort studies with follow-up rates indicated

Study	Location	Year commenced	Years of Follow up	Follow-up rate (%)	Age at Baseline	Reference
Nakuru Eye Disease Cohort Study	**Kenya**	**2007**	**Baseline 6**	**- 50**	**50**	(25)
Beaver Dam Eye Study	USA	1988	Baseline 5 10 15	- 75 56 43	43-86	(10-12)
Blue Mountain Eye Study	Australia	1992	Baseline 5 10	- 64 53	49+	(13)
Rotterdam Study	Netherlands	1990	Baseline 2 6.5 11	- 77 53 37	55+	(14, 15)
Copenhagen City Eye Study	Denmark	1986	Baseline 14	- 38	60-80	(16)
Barbados Eye Study	Barbados	1987	Baseline 4 9	- 74 60	40+	(17, 18)
Pathologies Oculaires Liees a L'Age	France	1995	Baseline 3	- 64	60+	(19)
Melbourne Visual Impairment Project	Australia	1992	Baseline 5	- 64	40+	(20)
Hisayama Study	Japan	1998	Baseline 5 9	- 65 -	40+	(21, 22)
Reykjavik Eye Study	Iceland	1996	Baseline 5	- 81	50+	(23)
Los Angeles Latino Eye Study	USA	2000	Baseline 4	- 73	40+	(24)

The major strengths of this study include the study design and use of state-of-the-art ophthalmic equipment for the examinations. All participants underwent testing on each station, regardless of visual status (a limitation of RAABs, the Nigeria National Survey and some aspects of the baseline study). This included:

- LogMAR Presenting Visual Acuity
- Autorefraction
- LogMAR Corrected Visual Acuity
- Visual Fields
- Anterior Segment Slit Lamp examination
- Goldmann Applanation Tonometry for Intraocular Pressure
- Gonioscopy
- Visual Fields
- Retinal photography
- Slit Lamp lens assessment (mydriatic)
- Anthropometry (height, weight, hip circumference, waist circumference, bioimpedance, blood sugar, HbA1c, blood pressure)
- Risk factor analysis (detailed questionnaire in the local language)

Furthermore, an ophthalmologist was available at both baseline (WM) and follow-up (AB) to confirm diagnoses, with independent verification through the Moorfields Grading Centre where image data was available. Methodological rigour of this cohort study is therefore on a par with existing ophthalmic cohort studies.

Much of the data from this cohort is now in the public domain and more will become so in the near future. This adds to our collective understanding of the epidemiology of eye disease in SSA, however further questions remain unanswered and for completion this data needs to be summarised and provided to the Ministry of Health in Kenya. A workshop has been proposed for 2018, which will bring together leading eye health researchers and policy makers in Kenya to discuss the findings and their implication for practice going forward.

Public Health Implications for Kenya

In line with the aims of the VISION2020 initiative, there has been major success reducing blindness from communicable diseases in the region, however cataract remains the leading cause of blindness.(26) The incidence of visually impairing cataract demonstrates the need to increase the current provision of eye services to meet the growing numbers of people losing sight from cataract and preventing the prevalence from growing as well as number of people who die never having had treatment.

Based on the data from this cohort study, the CSR needs to be between 232 and 4,298 cataract operations per million per year depending on those in the population for whom services are targeted. It should be noted that when targeting the most severely impaired group (bilaterally blind) those less severely impaired are identified also and so the case mix will usually include a variety of different levels of impairment (from experience, for every bilaterally blind person there will be 5-10 non blind persons on the operating list). Current estimates are that the CSR is around 550 / million / year. A target CSR of 2,000 has been set and for this to be achievable a long-term strategy to increase and retain ophthalmologists and cataract surgeons is needed as well as short and medium term solutions to maximise the reach and efficiency of existing human resources.

Posterior segment eye diseases are growing with the aging population and will contribute more to the burden of sight loss as measures to control cataract

strengthen.(26) These diseases are more complex in their presentation and management and will require a different approach to that alone of establishing strong cataract services.

Posterior segment eye diseases (PSED) are becoming more prevalent with the aging population with the need for cost-effective methods for identification and intervention to prevent sight loss becoming urgent.(2) Well resourced health systems are struggling to meet the growing demand of these non-communicable, chronic diseases that require frequent follow-up, intensive use of specialist equipment and personnel. The challenge is compounded as these diseases do not have interventions that restore or improve sight, but rather prevent progression to significant sight loss.

Diabetic retinopathy (DR) is a growing concern and whilst the prevalence and incidence is relatively low compared to other conditions in this population this is likely to change with the rapid epidemiological transition that is underway. (27) Effective management of DR must be tackled at the source, i.e. prevention of diabetes, rather than approaching it solely as an ophthalmic issue. A lack of awareness of risk factors for diabetes and an increasingly obesogenic environment are becoming critical issues that for a minority result in end stage organ damage including sight-threatening diabetic retinopathy. Greater demand is likely to be felt by eye care services as those in urban areas and of higher socioeconomic status are both more likely to become diabetic and more likely to have access to services. This perceived increase in demand by service providers needs to be balanced by the public health concerns and in particularly the large groups of the population for

whom accessing any services is difficult. Three key areas of systems strengthening is required to meet the growing number of people with potential sight loss from their diabetes, these are, but not limited to: (1) increasing service capacity (human resources and appropriate equipment for diagnosis and treatment), (2) increasing demand for services by creating awareness in those known to have diabetes about the risk of sight loss and potential for sight saving treatment with regular screening and follow-up, and (3) great efforts need to be made to reduce the incidence of diabetes by creating public awareness and policy changes that encourage a healthy environment.

Age related macula degeneration (AMD) is more prevalent in this population than many anticipated (7) however it is yet to be a major contributor to vision loss, in part due to the life expectancy of the population meaning many do not reach the age groups in which vision loss begins to manifest from AMD. AMD is not a priority public health concern yet as the prevalence of sight loss from AMD is low and effective treatments that prevent and restore vision are limited. This is likely to change in decades to come as cataract and refractive errors are better controlled and treatment options become more readily available.

Glaucoma identification continues to prove to be challenging to identify, even with modern equipment such as was available in this cohort. The standardisation of classifying glaucoma using the ISGEO criteria (28) for prevalence surveys has enabled comparative data across populations, however there is a need to develop a practical set of standards for identifying patients with, and monitoring progression of, glaucoma in settings where access to modern equipment is not feasible. This might

include a combination of simple tools to measure structural and functional optic nerve damage such as optic disc imaging, visual acuity testing, relative afferent pupil defect assessment and portable intraocular pressure measurement.

Effective reduction of blindness and visual impairment should also focus on reducing the barriers that currently exist, as demonstrated (Chapter 11) by the low uptake of services in those identified at baseline with operable cataract. (29-32) This should include a focus on:

- **A**wareness – many visually impaired people are not aware they have a treatable condition and therefore do not consider accessing services
- **B**ad Service – poor outcomes and limited availability of services
- **C**osts – the lowest socioeconomic groups are the most likely to be affected and both direct costs of treatment and indirect costs are unaffordable
- **D**istance – the location of services is often prohibitively far both in terms or time and cost to travel
- **E**scort – the need to have a carer take the potential beneficiary to the services creates a dependence on a family or community member
- **F**ear – potential beneficiaries are afraid of being in an alien environment when they already have lost their independence. Certain ideas around what happens at surgery can result in the rejection of services
- **G**ender – females are disproportionally more likely to not access services

Overall, the combination of cataract and PSED challenges requires a health system strengthening approach with the priority being the immediate issue of cataract visual impairment and longer-term concern of PSED. Both supply (treatment services) and

demand (improved access to those services) needs targeted changes including consideration of novel approaches such as task-sharing and task-shifting (33) to create efficiencies that enable a higher volume and quality of services. This includes empowering community workers and volunteers to be involved in sensitization and case finding and providing more basic eye services closer to the patient's homes to increase access and raise demand as well as establishing policies that are supportive of new cadres delivering tasks previously limited to the scope of established cadres. Sensitivity is needed to ensure that those from established cadres do not feel threatened and in fact support these initiatives and are provided with assurance that their roles are protected and will in all likelihood become more demanding due to the increased workforce closer to the population who remain off the medical grid.

Based on the finding of this body of work, it is recommended that the focus of VISION2020 remains that of tackling avoidable blindness and visual impairment through delivery of high volume, high quality cataract and refractive error services and that the emerging posterior segment eye diseases should not distract from this focus. Health care system strengthening, including eye health systems is required of PSEDs are to be managed once cataract and refractive errors come under better control.

Future work

This population-based cohort study from Nakuru, Kenya, has huge amounts of untapped information that warrants analysis, interpretation and sharing.

Outside the scope of this thesis, many other manuscripts are being prepared and several others will be developed in due course.

The list below is a summary of these.

Manuscripts under review or in preparation:

1. Reference values for body composition and associations with blood pressure in Kenyan adults [under review]

2. Changes in the magnitude and pattern of socioeconomic inequality in blindness and visual impairment in Nakuru County, Kenya between 2007/08 and 2013/14

3. The incidence and risk factors for hypertension in a population-based cohort of older people in Kenya

4. The incidence of obesity and potential risk factors in a population-based cohort of older people in Kenya

5. The incidence of sub-types of lens opacity in a population-based cohort of older people in Kenya

6. The incidence of posterior capsular opacification in a population-based cohort of older people in Kenya

7. The prevalence and incidence of pterygium and corneal opacities in a population-based cohort of older people in Kenya

8. Risk factors for mortality from a population-based cohort of older people in Kenya

9. Mortality and visual impairment in a population-based cohort of older people in Kenya

10. Comparing various models of calculating incidence from prevalence data and its validity in the Nakuru Eye Disease Cohort

11. HbA1c in population-based sample of Kenyan adults.

Peek

Multiple challenges were faced throughout this cohort study such as a lack of infrastructure (poor roads, unavailability of electricity) and dependence on highly skilled personnel to deliver the examinations and data demonstrating the big gap between accessible services and need for services.

Peek was designed to overcome, or reduce some of these challenges by enabling task shifting to more available cadres of the workforce and create the possibility for roles to be performed by people who do not typically have a role in health service delivery (e.g. community volunteers and teachers). The design and validation of these tools was nested within the cohort study and included the validation of a smartphone visual acuity test, Peek Acuity (34) and a smartphone retinal imaging adapter, Peek Retina. (35) The acceptability of these tools was assessed and found to be highly acceptable by patients, examiners and key stakeholders. (36)

Peek could potentially be used to help overcome three major challenges identified in this thesis:

1. Increase the availability of data on the prevalence of PSED in Africa

These tools are now being embedded into survey tools, including mRAAB, an evolution of the Rapid Assessment of Avoidable Blindness methodology (4) to increase the quality of data being collected in surveys to support understanding the eye health needs at a district level including disaggregated PSED and planning modules that combine a needs assessment (prevalence) with a resource assessment (capacity) to deliver achievable plans.

2. Identify people in the community who need eye services and lower barriers to them accessing them

Tools and methodologies are also in development and implementation to lower many of the barriers to accessing services experienced in this cohort study, including Community Screening, School Screening (37) and Diabetic Retinopathy Screening.(38) These systems utilise connected Peek tools to connect those identified in the community with appropriate services as well as enabling real-time feedback to all those involved in the patient care pathway including carers, local opinion leaders and programme managers. Further information is available from: https://www.peekvision.org/peek-systems/

Table. Summary of locations at which key activities (identification, triage and treatment) take place in the different models

System	**Identify**	**Triage**	**Treat**
School	Schools	Local camps or in the school	Local camp/refractive service/hospital
Community	Households	Primary health care facilities	Hospital
Diabetes	Primary health care facilities	Cloud based	Hospital

3. Increase the capacity in ophthalmic institutions

Many ophthalmic institutions in SSA are poorly resourced. Peek tools such as the smartphone based visual acuity test, Peek Acuity, and Peek Retina for assessing the fundus can be used to provide additional capabilities. They can also be used in end-to-end solutions that mean less time is spent by highly-trained specialists performing tasks that can be performed by other cadres.

Further information on Peek is available in the appendix.

Conclusions

The incidence of visual impairment and blindness in Nakuru Kenya is high and the majority of people in who are blind are avoidably so. Strengthening of the health system is required if sustainable change is to be delivered.

Short-term efforts should continue the efforts of VISION 2020 to focus on controlling cataract visual impairment. In the long-term, the focus must shift to whilst building capacity to identify and manage posterior segment eye diseases early.

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APPENDICES

Appendix I - Ethical Approval from LSHTM

Appendix II - Peek

Appendix III - Published papers on Peek

Appendix IV - Published papers from the baseline study

Appendix I – Ethical Approval from LSHTM

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LONDON SCHOOL of HYGIENE &TROPICAL MEDICINE

Observational / Interventions Research Ethics Committee

Dr Andrew Bastawrous
International Centre for Eye Health
CRD/ITD
LSHTM

26 June 2012

Dear Dr Bastawrous,

Study Title: **The Incidence and Progression of Posterior Segment Eye Diseases in Nakuru, Kenya**
LSHTM ethics ref: **6192**

Thank you for your email of 20 June 2012, responding to the Observational Committee's request for further information on the above research and submitting revised documentation.

The further information has been considered on behalf of the Committee by the Chair.

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised, subject to the conditions specified below.

Conditions of the favourable opinion

Approval is dependent on local ethical approval having been received, where relevant.

Approved documents

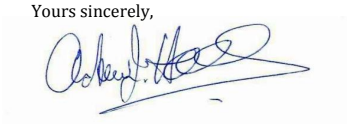
The final list of documents reviewed and approved by the Committee is as follows:

Document	Version	Date
LSHTM ethics application	V2	13/06/2012
Protocol	V3	14/06/2012
Information Sheet	V2	13/06/2012
Consent form	V2	13/06/2012

After ethical review

Any subsequent changes to the application must be submitted to the Committee via an E2 amendment form. All studies are also required to notify the ethics committee of any serious adverse events which occur during the project via form E4. At the end of the study, please notify the committee via form E5.

Yours sincerely,



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Appendix II – Peek

Appendix II. Peek

In the two years prior to commencing the fieldwork required for this PhD study I began reviewing all the equipment, personnel and training that would be required to deliver the study effectively. As preparation for the application and subsequent interview with the Medical Research Council and Fight for Sight (who went on to fund the PhD Fellowship) I began assessing any alternative ways the follow-up could be done given the half decade of progress since the baseline study. Although there were some updates and marginal changes in equipment available, the fundamental challenges that were present at baseline remained true at follow up: most of the 100 clusters did not have access to a stable power supply, three-quarters were not accessible on tarmac road and the equipment required specialist training to use appropriately and was all at risk of failure as they were designed for use in an environment that is dust free, with minimal temperature variation and stable power supply. Furthermore, most of the equipment was designed to be stationary rather than moved, unpacked and repacked several times per week.

I had received feedback that the cohort was unlikely to be funded, although the work was of high scientific importance the challenges delivering it meant this was considered a high-risk study. Fortunately the Medical Research Council and Fight for Sight were convinced that the study could be delivered, nonetheless, I continued to explore ways it may be less logistically challenging to deliver.

While writing my first draft of the PhD application I purchased my first smartphone and like the many early adopters before me soon realised I had something that was going to fundamentally change the way we communicated. I also realised that the

impressive computing power, high resolution screen, in-built camera and constant "connectedness" meant this could be harnessed for delivering ophthalmic examinations. Assuming this is something that had already been done I began downloading as may "eye test" apps as I could find, hoping there may be something I could use as an alternative to all the equipment I was going to need to buy. To my disappointment they were all unsuitable. With some colleagues we began systematically reviewing every one of the apps available at the time concluding that they were almost all unvalidated and not suitable for use in clinical practice. (1) Searching the wider mHealth landscape, beyond eye health there were several examples of effective mHealth apps, hardware or services being used. (2) These included a mobile phone base clinical microscopy tool (3) which led me to believe it must be possible to image the retina with a smartphone.

Given the anticipated logistical challenges that lay ahead for my PhD and those who might attempt to replicate it, I began prototyping smartphone vision tests and hardware adaptions for retinal imaging. My first successful attempt to view the retina with my smartphone was adapting the indirect technique, which uses a co-axial light source mounted on a hat between the examiner's eyes and a condensing lens. By using a smartphone in video mode with the flash on I was able to get fundus views effectively. (4) Its use was limited to only being effective in the hands of an ophthalmologist and so I begun working on several other prototypes with help from engineers with specialist experience. After several unsatisfactory attempts to make something usable by a non-specialist, an engineering colleague in the university collaboration we had established, successfully 3D printed a device that was easy to use and provided satisfactory images in the hands of a non-specialist. (5) We developed multiple further prototypes before establishing a nested study within the

cohort to validate its use in the hands of a non-physician against the reference standard desktop retinal camera being operated by an ophthalmic technician. Images from both were independently graded at Moorfields Eye Hospital Reading Centre. When performing an optic disc grading the two techniques were found to be comparable. (6) In parallel multiple prototypes of a visual acuity Android app had been tested and improved with a similar ambition of making it possible to accurately measure visual acuity in the hands of a non-physician. As with retinal examinations, this was nested within the cohort study and examiners were asked to measure participant's vision at home and repeated again in the clinic the following day where they also underwent the reference standard vision test on an ETDRS chart. An experienced clinical officer undertook the reference standard vision test in controlled conditions. The visual acuity app, in the hands of a lay-user, was found to be as accurate as ETDRS, as repeatable as Snellen and quicker than both. (7)

As well as validity testing both the acuity app (Peek Acuity) and the retinal hardware (Peek Retina), the adoptability and acceptability of these tools were assessed through qualitative interviews with patients, examiners and stakeholders. The conclusions from the in-depth interviews were that, "Peek is an acceptable solution, as it provides a beneficial service, supports patients' needs, and fulfils health care providers' roles, overall contributing to strengthening eye health". (8)

The app has consequently been released globally and is now been using in 126 countries. It's use has been independently validated in several settings, including Aravind Eye Hospital in India where it was chosen as the acuity app of choice for use within in a local trial (personal correspondence).

The ambition was not to create stand-alone tools such as a vision test or smartphone ophthalmoscope, it was to create tools that could be integrated in to digital data collection tools enabling greater access to services for those most in need and least likely to receive services, and to make research more straight-forward than it was anticipated to be and without question proved to be. The integration of these tools could be specifically for remote interpretation of retinal images or more comprehensive workflow integration. (9, 10)

The fist scenario in which integrating these tools were applied, was within a school screening program in Kitale, Kenya. It was estimated that one on 20 children in school had an undetected visual impairment and most schools had no active school screening facility. The only active program required an eye nurse to leave the hospital and travel to neighbouring schools to conduct basic eye and vision assessments. It was found to be ineffective for several reasons: the ophthalmic nurses workload at the hospital increased in their absence as there was no back up provision; the majority of children screened in the schools, 19 in 20, did not have a vision problem but still required a specialist nurse assessment to discover this; and those were positively identified as needing review in the hospital were unlikely to attend despite referral (estimated at 10% attendance). Peek Acuity was tested in the hands of teachers and shown to be an effective way of positively identifying school children with visual impairment (data in preparation for publication). A screening system was developed to pull data on children who had screened positive and automating text messaging to their parents notifying them of assessment and need for hospital follow up. A cluster randomised control trial including over 20,000

children equally divided in to two arms, the Peek School Screening System and standard care (Card based vision assessment in the hands of the same teachers and letter referral). The adherence to referral in the intervention arm was 52% compared to 21% in the control arm (data in preparation for publication). The program has subsequently been adopted in Trans Nzoia County and is now scaling to reach 300,000 children. The program has also been replicated in Botswana with a recent pilot completed and plans underway for a national program to commence next year. A further cluster randomised control trial of Peek School Screening is underway in India. (11) Further work is underway developing or collaborating on the development of:

- Contrast sensitivity
- Red desaturation
- Visual fields
- Colour vision

And systems that use Peek Acuity, Peek Retina and potential other Peek developed or third party apps in connected systems for:

- School screening
- Community screening
- Population surveys
- Diabetic Retinopathy screening

In the course of this PhD, Peek has grown from an idea to a suite of software apps, hardware and systems, (12) some globally available and other continuing validation and trials. A spin out from the London School of Hygiene & Tropical Medicine was

established in 2015. The Peek Vision Foundation, a UK Charity to mission lock the purpose of Peek as an organisation that represents the millions of people avoidably visually impaired. A wholly owned subsidiary trading company, Peek Vision Ltd has been established as a legal manufacturer of medical devices and is working to become a sustainable provider of products and services that radically increase access to eye care services. Profits from the company are gifted to the Foundation to further build eye care capacity in low and middle-income countries.

The following short essay was submitted to and was selected as the winner of the Medical Research Council, Max Perutz Science Writing Award:

Why Does My Research Matter? – Max Perutz Science Writing Award

Everything is hazy; He keeps his eyes closed; it doesn't seem to make much difference opening them. His hand clumsily feels around the bedside table reaching for his mobile phone and knocking last night's cold mug of tea to the floor. Today is the day he hopes he'll get his sight back

Losing sight is the sense most people fear losing most. I am privileged to be in a profession (ophthalmology) where centuries of research and practice have brought us to a time when so much of blindness is now curable or preventable. There is no feeling like it when the eye patch comes off someone who hasn't seen for years, the sheer wonder as they take in their surroundings and their anticipation to see faces that have become voices and places that have become memories.

Incredibly, despite 80% of blindness being curable or preventable, the majority of blind people with treatable eye conditions live in developing countries and have no access to suitable healthcare. Africa has the greatest disparity in numbers needing treatment and specialists available to provide it. For example, in the UK we have 3,600 ophthalmologists (eye surgeons/doctors) compared to only 86 in Kenya where I will be moving to later this year.

There are many factors that can lead to blindness, and many complexities that lead to a society unable to deal with the burden that comes with a disability. Although each individual goes blind very much alone, there are shared stories and features, the understanding of which can enable prevention or access to curative treatment. Some of the major questions include knowing *how many* people are blind? *Who* are they? *Where* do they live? *Why* are they blind? At *what rate* are people becoming blind? All

this information is vital for planning a health service and using limited resources in a way that will allow the maximum number of people to receive treatment and restore or preserve their vision.

Gathering this type of information is known as epidemiological research, it is a method of describing the characteristics of a population. This information is then used in practice to inform policy makers and health workers to benefit individuals on a large scale.

Performing such a study can be a logistical nightmare, it is also extremely time consuming and expensive. My study involves the retracing and examination of 5,000 people across a district in Kenya known as Nakuru. Taking what is effectively a fully staffed eye hospital (team of 15 people), fully equipped (over £100,000 worth of heavy and fragile equipment) to remote villages, many of which have no road access or electricity supply is extremely challenging yet absolutely vital if provision to prevent needless blindness is to be put in place.

As I've pondered and planned for the challenges that lay ahead, I've had the continual thought that there must be an easier way to gather this information, a way that is less expensive, less resource hungry and therefore could be used on a much wider scale. Then it dawned on me… I use my smartphone for everything nowadays, from checking train times, navigating in the car, taking and sharing photos, not to mention using it as a phone and speaking to people. This has led me to develop a set of gadgets and applications making it possible to use a modified smartphone (I call it the Eye Phone) to measure someone's vision, check their refractive error (glasses prescription), take photos of the back of the eye for diseases such as diabetic retinopathy, macula degeneration and glaucoma and check for the presence of a cataract. All the data is then stored on the phone and can be shared with specialists anywhere in the world to provide expert diagnosis and treatment plans in even the most remote locations. Individuals are locatable on an interactive Google Map, and can be retraced and contacted to arrange treatment or follow up.

It is important to check the new device works and doesn't miss people who need help. To see how accurate the new device is, I will test it on the same 5,000 individuals undergoing the detailed examinations that use the gold-standard state-of-the-art hospital equipment with the phone also. We will then be able to compare the two methods and see how many of the study population we would have correctly picked up as having sight loss (as well as the reasons why) and if we would have missed anyone. At one-fiftieth of the price and only one non-specialist needed to perform the test, the examiner can go to the patient rather than the patient waiting for someone to never come. It could mean those in difficult to reach places, silently losing their sight, could be a text message away from help.

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Appendix III – Published papers on Peek

1. Development and Validation of a Smartphone-Based Visual Acuity Test (Peek Acuity) for Clinical Practice and Community Based Fieldwork [8p]
2. Clinical Validation of a Smartphone-Based Adapter for Optic Disc Imaging in Kenya [7p]
3. Analysis of Eye Care Services in Kenya and the Acceptability, Usability, and Views on Deployment of Peek, a Mobile Phone mHealth Intervention for Eye Care:A Qualitative Study [14p]
4. Increasing access to eye care . . . there's an app for that. Peek: smartphone technology for eye health (photo essay) [4p]

Original Investigation

Development and Validation of a Smartphone-Based Visual Acuity Test (Peek Acuity) for Clinical Practice and Community-Based Fieldwork

Andrew Bastawrous, MRCOphth; Hillary K. Rono, MBBS; Iain A. T. Livingstone, FRCOphth; Helen A. Weiss, PhD; Stewart Jordan, BSc; Hannah Kuper, ScD; Matthew J. Burton, PhD

IMPORTANCE Visual acuity is the most frequently performed measure of visual function in clinical practice and most people worldwide living with visual impairment are living in low- and middle-income countries.

OBJECTIVE To design and validate a smartphone-based visual acuity test that is not dependent on familiarity with symbols or letters commonly used in the English language.

DESIGN, SETTING, AND PARTICIPANTS Validation study conducted from December 11, 2013, to March 4, 2014, comparing results from smartphone-based Peek Acuity to Snellen acuity (clinical normal) charts and the Early Treatment Diabetic Retinopathy Study (ETDRS) logMAR chart (reference standard). This study was nested within the 6-year follow-up of the Nakuru Eye Disease Cohort in central Kenya and included 300 adults aged 55 years and older recruited consecutively.

MAIN OUTCOMES AND MEASURES Outcome measures were monocular logMAR visual acuity scores for each test: ETDRS chart logMAR, Snellen acuity, and Peek Acuity. Peek Acuity was compared, in terms of test-retest variability and measurement time, with the Snellen acuity and ETDRS logMAR charts in participants' homes and temporary clinic settings in rural Kenya in 2013 and 2014.

RESULTS The 95% CI limits for test-retest variability of smartphone acuity data were ±0.029 logMAR. The mean differences between the smartphone-based test and the ETDRS chart and the smartphone-based test and Snellen acuity data were 0.07 (95% CI, 0.05-0.09) and 0.08 (95% CI, 0.06-0.10) logMAR, respectively, indicating that smartphone-based test acuities agreed well with those of the ETDRS and Snellen charts. The agreement of Peek Acuity and the ETDRS chart was greater than the Snellen chart with the ETDRS chart (95% CI, 0.05-0.10; $P = .08$). The local Kenyan community health care workers readily accepted the Peek Acuity smartphone test; it required minimal training and took no longer than the Snellen test (77 seconds vs 82 seconds; 95% CI, 71-84 seconds vs 73-91 seconds, respectively; $P = .13$).

CONCLUSIONS AND RELEVANCE The study demonstrated that the Peek Acuity smartphone test is capable of accurate and repeatable acuity measurements consistent with published data on the test-retest variability of acuities measured using 5-letter-per-line retroilluminated logMAR charts.

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Visual acuity (VA) is the most frequently performed measure of visual function in clinical practice. Visual acuity measurements are used to establish the need for clinical investigation and quantify changes in central vision over time.

Four percent of those who attend general practice in the United Kingdom do so with an eye problem[1] and a formal measure of VA should be part of each of these consultations.[2] Globally, 285 million people have visual impairment, with 80% having diseases with known curative or preventive treatment. However, most live in low-income countries with minimal access to detection and subsequent treatment.[3]

The Snellen chart[4] is the most common method for the measurement of VA in ophthalmic and general practice; however, it is limited by the nongeometric progression in letter sizing from line to line and the inconsistent number of letters per line.[5] Different letters or optotypes (standardized symbols for testing vision) have varying legibility at the same size and secondary effects, such as crowding, are known to affect the ability of the patient to determine optotypes correctly and therefore could lead to measurement bias.

The limitations of the Snellen chart have largely been overcome with the development of logMAR acuity charts,[6] which are now frequently used in clinical research, such as the Early Treatment Diabetic Retinopathy Study (ETDRS) charts. Despite this improvement, the Snellen chart remains the dominant method for acuity testing in clinical practice.[7] This may be owing to several factors including familiarity, a well-recognized scoring system, smaller chart size, and the speed of performing the test relative to the ETDRS chart test.

Mobile telephone technology has evolved rapidly in recent years. In 2013, an estimated 280 million (20%) of the 1.4 billion mobile telephones sold were smartphones and this proportion is expected to increase, particularly in low-income settings,[8] where fixed-line technology has been leapfrogged straight to mobile technology,[9] providing the potential to access health care without the previously required infrastructure.[10]

The medical community is embracing mobile technologies with its potential in health care information delivery, real-time patient monitoring, research data collection, and mobile telemedicine for the provision of expertise to remote locations.[10]

We hypothesized that a logMAR-style smartphone-based vision test (Peek Acuity), with a fast-testing algorithm, would allow measurements to be made in a clinically acceptable time, with greater precision and reliability than is possible with Snellen charts. Visual acuity results can be displayed in familiar Snellen chart notation (imperial or metric) or logMAR.

The Peek Acuity test was developed and compared, in terms of test-retest variability (TRV) and measurement time, with the Snellen chart and the ETDRS-based tumbling E logMAR chart (reference standard) in controlled and uncontrolled (real-world) settings in rural Kenya.

At a Glance

- Visual acuity is an important measure of visual function, necessary for decision making with ophthalmic patients. This research aimed to develop and validate a smartphone-based visual acuity application.
- Peek Acuity appeared to be comparable in repeatability and speed with Snellen acuity.
- Peek Acuity appeared to be comparable with Early Treatment Diabetic Retinopathy Study logMAR for measuring visual acuity.
- Peek Acuity appeared to be reliable for in-home and in-clinic assessment of visual acuity.
- Accurate measures of visual acuity can be performed by nonhealth care personnel using Peek Acuity.

Methods

Participants

This study, conducted from December 11, 2013, to March 4, 2014, was nested within the 6-year follow-up of the Nakuru Eye Disease Cohort in central Kenya, a population-based study that recruited 5000 individuals from 100 clusters in 2007 selected through probability proportionate to the size of the clusters, with individuals sampled within clusters through compact segment sampling.[11,12] Follow-up of the participants was undertaken in 2013 and 2014.[12] Three hundred consecutive participants from the final 21 survey clusters who were undergoing reference measures of VA as part of the cohort follow-up were invited to enroll into this additional study of alternative VA measures. A temporary mobile eye clinic was set up in the center of each cluster. All participants examined in the study were aged 55 years and older.

Ethics Approval

The study adhered to the tenets of the Declaration of Helsinki[13] and was approved by the ethics committees of the London School of Hygiene and Tropical Medicine and the African Medical and Research Foundation, Kenya. Approval was sought from administrative heads in each cluster, usually the village chief, who were given a copy of the consent form to read and pass on to those in the village.

Informed consent was obtained from all participants. The objectives of the study and examination process were explained in the local dialect in the presence of a witness. All participants gave written (or thumbprint) consent to participate.

Peek Acuity Test

The Peek Acuity application was written in Android and, for the purposes of this study, was used on a Galaxy SIII GT-I9300 (Samsung C&T Corp) running Android 4.0. The application was directly installed onto the test devices. Screen brightness was set to 100% within the application and all other options detailed here are built in.

Peek Acuity follows the standard ETDRS chart design with a 5 × 5 grid optotype letter E displayed in 1 of 4 orientations (90°, 180°, 270°, and 0°). The participant points in the direction they perceive the arms of the E to be pointing and the tester uses the touch screen to swipe accordingly, translating the gestures from the patient. The tester is masked to the presented optotype and is unaware whether the participant is providing the correct response. This method reduces verbal or nonverbal clues, which may bias the result. Single

optotypes are shown to reduce confusion; however, a bounding box is used to simulate the crowding effect of a standard ETDRS chart using a crowding bar, with thickness equivalent to the limb of the optotype, and spacing between optotype and crowding bar equal to that of half the total optotype size. This contour interaction format matches that used by the reference standard ETDRS chart. A stair-casing algorithm is used to simulate clinical practice for time efficiency.

Peek Acuity offers standardized alternatives to count fingers, hand movements, and light perception. For count fingers, the application randomly presents between 1 and 4 bars and a correct or incorrect response is recorded on screen. For hand movement, a solid black box, half the width of the screen, moves backward and forward across the screen. For perception of light, Peek Acuity switches on the telephone's LED flashlight and the participant is asked to identify if and when they see the light come on and off, with the option to assess for perception of projection direction. Test completion is indicated by a sound and vibration alert.

Visual acuity results can be displayed in logMAR or metric or imperial Snellen units based on user preference. An additional option, SightSim, presents a live video feed with a gaussian blur equivalent to the outcome of the vision test (eFigure 1 in the Supplement), which is of value in sharing the information with those not familiar with acuity scoring.

Visual Acuity Measurement

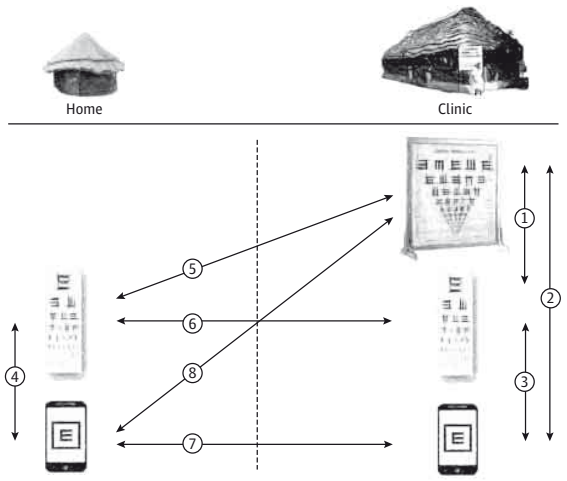
Paired VA measures were made in both the participant's home and in the central clinic on 2 consecutive days. For all tests, the presenting acuity was measured, with habitual correction if worn. On day 1, a health care worker with basic eye care training and a field worker without formal health care training visited participants in their homes. The participants were tested using (1) Peek Acuity (logMAR units) at 2 m and (2) a reduced 3-m tumbling E Snellen chart (Sussex Vision) inside or close to the participant's home (eFigure 2 in the Supplement). The order of the test was determined randomly by coin toss. The detailed testing procedures are described in the eAppendix in the Supplement.

On day 2, the participants seen on day 1 were reassessed in the cluster's central clinic. The same personnel retested the study participants using (1) Peek Acuity (logMAR units) at 2 m and (2) a reduced 3-m tumbling E Snellen chart to allow for measures of TRV. The order of the test was determined randomly by coin toss. The ETDRS VA was measured using a back-illuminated 4-m ETDRS chart (Precision Vision Inc) (eFigures 3 and 4 in the Supplement) by an ophthalmic clinical officer, which is the reference standard for this study. All testing (ETDRS, Snellen, and Peek Acuity) at the different cluster clinic sites was standardized: conducted indoors, the test area was screened with blackout curtains, and there were controlled ambient light levels within a range of 80 to 300 lux (ISO-TECH: ILM1332A light meter), in accordance with British standards for acuity assessment.[14]

Statistical Analysis

In total, 8 comparisons of the various VA measures in the different settings were made (**Figure 1**).

Figure 1. Testing Regimen of Peek Acuity, Snellen, and LogMAR in the Participants' Homes and in Clinics



1 represents Early Treatment Diabetic Retinopathy Study (ETDRS) in the clinic (reference standard) vs Snellen in the clinic; 2, ETDRS in the clinic vs Peek Acuity in the clinic; 3, Snellen in the clinic (clinical norm) vs Peek Acuity in the clinic; 4, Snellen at home vs Peek Acuity at home; 5, ETDRS in the clinic vs Snellen at home; 6, Snellen at home vs Snellen in the clinic (test-retest variability); 7, Peek Acuity at home vs Peek Acuity in the clinic (test-retest variability); and 8, ETDRS in the clinic vs Peek Acuity at home.

For any pairwise comparison of methods, the TRV was estimated as 95% CI limits of agreement (mean paired difference between measures ±1.96 SD). Histograms of the distribution of the test-retest and between-test method variability data suggested that the data were consistent with a normal distribution. Scatterplots of the observed TRV plotted against the average of the difference between the test and retest measurements suggested that there were no systematic associations between TRV and the underlying bias relating to level of acuity. Therefore, the Bland and Altman[15] methods were used for (1) bias (mean and 95% CI of the mean) between ETDRS (reference test) and both Snellen and Peek Acuity scores and (2) TRV for the paired Snellen acuity and Peek Acuity scores. Mean time scores between Snellen and Peek Acuity tests were compared using paired *t* tests. Acuity scores were converted into a logMAR for data analysis. In the Supplement, eTable 1 outlines the logMAR scores used including where acuity was too poor to measure with optoytypes.[16]

Results

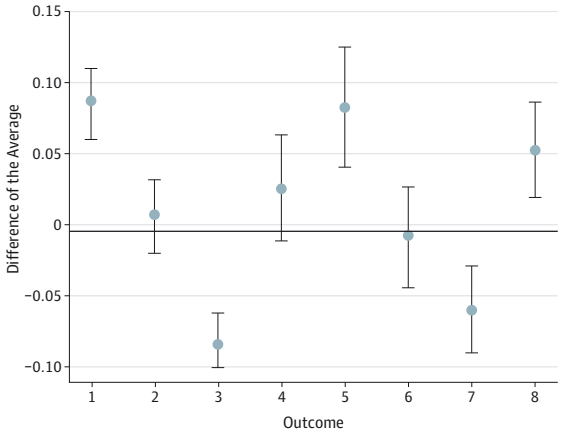
The Peek Acuity study took place between December 2013 and March 2014. Of the 300 participants selected, 293 enrolled (98%; 135 men and 158 women). In total, 272 people (91%; mean age, 65 years; range, 55-97) were examined and completed all 3 tests in the central clinic on day 2. Of these, 233 (86%) were available and had also taken both VA tests at home on day 1.

Table 1. Results of the 8 Pairwise Comparisons of the Right Eye Showing Bland-Altman and Pearson Correlation Analysis

Comparison	Participants, No.	Description	Difference of Average	95% CI Mean Difference	95% Limits of Agreement	Pearson Correlation Coefficient (95% CI)
1	272	ETDRS vs Snellen in the clinic	0.088	0.063 to 0.114	−0.329 to 0.506	0.932 (0.914 to −0.946)
2	272	ETDRS vs Peek Acuity in the clinic	0.011	−0.014 to 0.035	−0.396 to 0.417	0.936 (0.919 to 0.949)
3	272	Snellen in the clinic vs Peek Acuity in the clinic	−0.078	−0.100 to −0.056	−0.439 to 0.283	0.950 (0.937 to 0.960)
4	233	Peek Acuity at home vs Snellen at home	0.029	−0.007 to 0.065	−0.517 to 0.575	0.902 (0.875 to 0.923)
5	233	ETDRS vs Snellen at home	0.084	0.043 to 0.125	−0.541 to 0.709	0.865 (0.828 to 0.894)
6	233	Snellen in the clinic vs Snellen at home	−0.004	−0.038 to 0.030	−0.523 to 0.515	0.907 (0.881 to 0.927)
7	233	Peek Acuity at home vs Peek Acuity in the clinic	−0.054	−0.083 to −0.025	−0.498 to 0.390	0.933 (0.914 to 0.948)
8	233	ETDRS vs Peek Acuity at home	0.055	0.023 to 0.088	−0.438 to 0.549	0.917 (0.893 to 0.935)

Abbreviation: ETDRS, Early Treatment Diabetic Retinopathy Study.

Figure 2. Difference of the Average



The graph shows 8 outcomes (right eye), with difference of the average in logMAR on the y-axis and comparisons on the x-axis. 1 represents Early Treatment Diabetic Retinopathy Study (ETDRS) in the clinic (reference standard) vs Snellen in the clinic; 2, ETDRS in the clinic vs Peek Acuity in the clinic; 3, Snellen in the clinic (clinical norm) vs Peek Acuity in the clinic; 4, Snellen at home vs Peek Acuity at home; 5, ETDRS in the clinic vs Snellen at home; 6, Snellen at home vs Snellen in the clinic (test-retest variability); 7, Peek Acuity at home vs Peek Acuity in the clinic (test-retest variability); and 8, ETDRS in the clinic vs Peek Acuity at home.

The median VA measured by the ETDRS chart for all eyes tested (all levels of vision including those unable to read the ETDRS chart) was 0.23 logMAR, with a range of −0.2 to 4.0 logMAR (Snellen equivalents: median, 20/32; range, 20/12.5 to no light perception).

The results of the 8 pairwise comparisons of the right eye VA described here are presented in **Table 1** and **Figure 2**, with results for the left eye available in the eAppendix in the Supplement (no difference between the right and left eyes was found; eTable 2 in the Supplement). The comparisons of clinic-based Snellen and clinic-based Peek Acuity measures with the ETDRS chart under the standardized clinic conditions indicated that Snellen tests showed a high degree of correlation with the ETDRS chart but that this was higher still with Peek Acuity (95% CI, 0.05-0.10; P = .08). The mean difference between the Peek Acuity measure in the clinic and the ETDRS chart measure was 0.011 logMAR units (95% CI, −0.014 to 0.035) and 0.032 logMAR units (95% CI, 0.010 to 0.054) for the right and left eyes, respectively. This was equivalent to less than 3 letters on a line difference when taking the upper confidence limit of the mean difference. The correlation (scatter) plots and Bland-Altman difference plots for these comparisons in the right eye are shown in **Figure 3**A.

Comparing Peek Acuity tested at home with ETDRS testing in the clinic, the mean difference between the Peek Acuity score at home and the ETDRS score was 0.055 logMAR (95% CI, 0.023-0.088) and 0.072 logMAR (95% CI, 0.039-0.105) for the right and left eyes, respectively, which is equivalent to 5 letters or 1 line of difference (Table 1; Figure 3B).

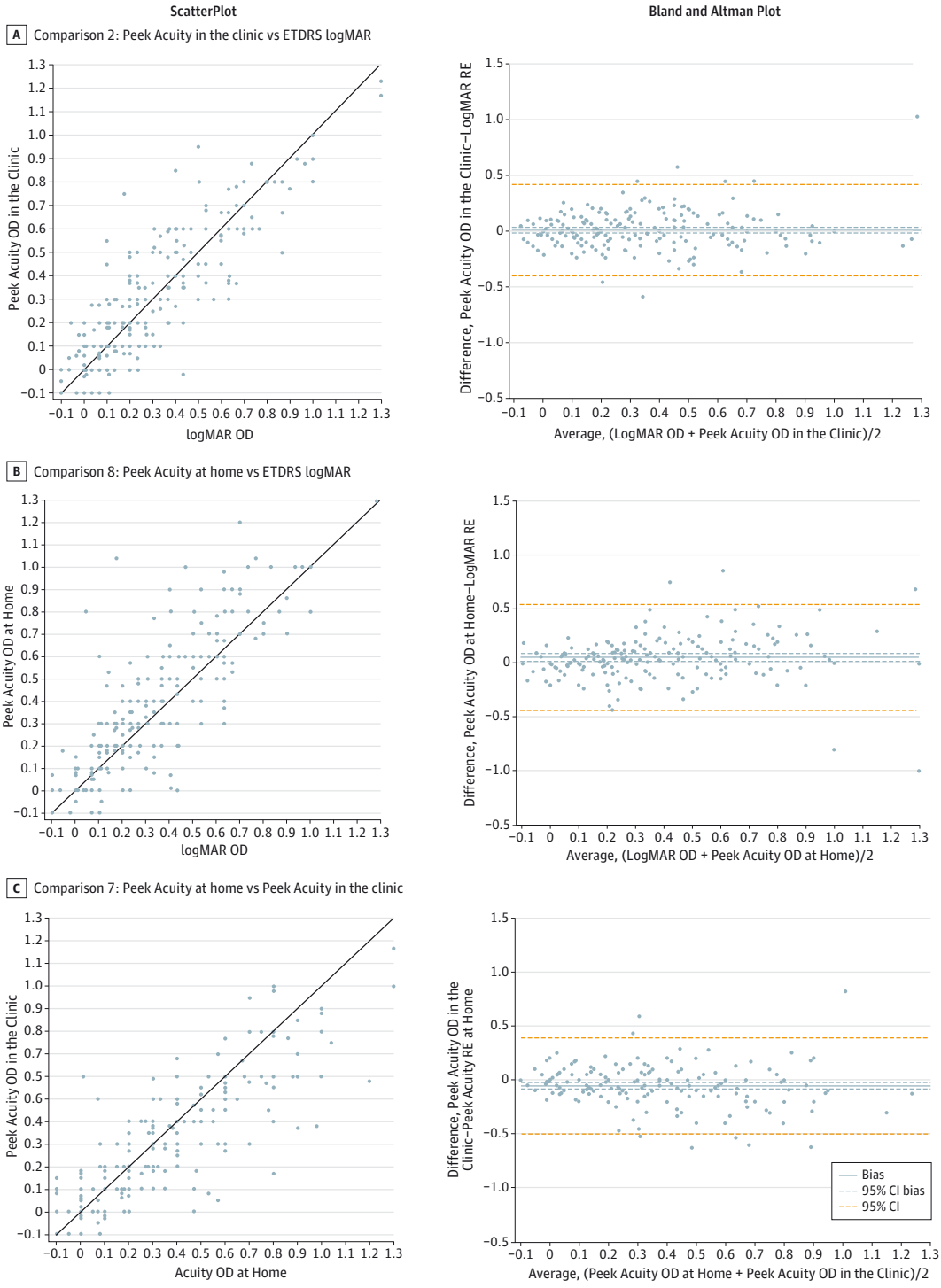
The Peek Acuity TRV (comparison 7 as indicated in Figure 1) performed by the same examiner on day 1 at home and on day 2 in the clinic had a high correlation and a small difference of averages (Table 1; Figure 3C).[17]

Mean testing time for both eyes on 126 study participants in whom testing time was measured was 82 seconds (95% CI, 73-91 seconds) with Snellen and 77 seconds (95% CI, 71-84 seconds) with Peek Acuity, showing no difference (P = .13).

Peek Acuity used at home by a community health care worker was 85% sensitive and 98% specific (eTable 3 in the Supplement) at detecting eyes with severe visual impairment (deemed locally as the surgical cutoff point for operable cataract; Snellen equivalent of ≤6/60) when compared with the ETDRS testing in controlled conditions. In addition, there was excellent agreement across World Health Organization vision categories between ETDRS and Peek Acuity when used at home (eTable 4 in the Supplement).

No adverse events from performing any of the acuity tests were reported.

Figure 3. Scatter and Bland and Altman Plots



The scatter and Bland and Altman plots for outcomes 2, 8, and 7 for the right eye (RE).

Discussion

The ubiquity of smartphones among health care professionals[18] and increasing penetration, particularly in low- and middle-income countries, provide potential for delivering high-quality, objective, repeatable, and acceptable vision testing throughout the world.

With most of the world's blind people living in low-income countries, the need for tools to increase early detection and appropriate referral are vital if the prevalence of blindness and visual impairment is to be reduced. In high-income settings, where primary care consultations are time pressured and confidence in diagnosing ophthalmic problems is low,[19] accessible tools to provide reliable measures to guide management are vital. The referral of patients with ophthalmic symptoms from primary care, such as in general practice or accident and emergency, to specialist care should include a measure of acuity that is reliable and accessible and further testing in these contexts is encouraged.

In this study, we aimed to develop and validate a smartphone-based VA test appropriate for use in challenging circumstances, such as rural Africa, as well as being reliable enough for use in routine clinical practice in well-established health care systems. Overall, Peek Acuity performed well and the testing time was no slower or less repeatable than with the Snellen test, while being comparable in accuracy to the ETDRS chart. For clinical and population screening use, the TRV of acuity should be consistent across the acuity range and measurable in terms of lines or letters of change; measurement error obscures true clinical change and reduces the statistical power of clinical trials using acuity as a primary outcome measure.[20] Peek Acuity testing proved to be repeatable and consistent. Our findings also indicated that the reduced Snellen chart is a repeatable and time-efficient VA test that still has application in clinical and field settings.

In our study, the TRV of the Snellen chart was higher than in comparable studies,[5,21] which may have been owing to tightly defined end points (no part scores were given for part completion of a line).

Although multiple applications for the testing of VA on smartphones are available, to our knowledge, most have not been tested for repeatability or reliability against a reference standard.[22] This study found Peek Acuity to be comparable with ETDRS-style chart, with similar TRV to that previously reported for other tests.[23,24] Key attributes and benefits for Peek Acuity are outlined in **Table 2**.

Table 2. Key Attributes and Potential Benefits of Peek Acuity

Key Attribute	Potential Benefits
Use of E optotype widens accessibility to those unable to read letters	Increased objectivity of test
Use of E optotype rather than letters ensures acuity is resolution based rather than recognition based	
Random optotype direction prevents learning effect from one eye to the other	
Automated visual acuity score calculation	
End-of-test indicator (vibration and sound alert)	
Gesture-based recording of responses, making the test more objective by swiping in the direction indicated while not seeing the letter and shake to record not seen	
Standardized low-vision measurement tools for count fingers, hand movements, and perception of light	Standardized testing and prompts for control of conditions
Ambient light sensor used for adjusting screen brightness and detecting threshold ambient light levels above which acuity measurements decrease in accuracy	
Use of ETDRS-based optotype with result available in all the standard units: decimal, logMAR, metric Snellen, and imperial Snellen	Easy interpretation of the results
Live video feed demonstrating appropriate level of gaussian blur according to outcome of the vision test (eFigure 1 in the Supplement), which is of value in sharing the information with those not familiar with acuity scoring	
Downloadable from the Google Play Store	Accessible and validated
CE marked (class I)	
Smartphone based	Potential to store data to an electronic patient record, increasing efficiency of data management and limiting potential recording error
	Data can be shared remotely with other health care professionals for feedback
	The electronic patient record can be geotagged, which is of particular value in resource-limited settings where addresses may not be available and patient follow-up is challenging

Abbreviation: ETDRS, Early Treatment Diabetic Retinopathy Study.

Low Vision

Low vision in participants who have VA below the level that can be measured on a chart are subject to assessment of vision that lacks a standardized approach and is open to considerable variability. In standard practice, if no optotypes are visible at the reduced distance, counting fingers is performed, followed by hand movements and finally differentiating between perception of light and no perception of light. In practice, this crucial measure of vision that may differentiate poor and good prognosis for treatment is often overlooked owing to these nonstandardized measures. Peek Acuity offers a standardized approach to testing such low levels of vision, which could be also performed on a tablet but was not assessed formally in this study.

Limitations

The study population comprised older-aged Kenyan adults, who may not be representative of other populations and age groups, limiting the generalizability. Other studies are ongoing to determine the suitability of this tool in different contexts across a range of different handsets and operating systems (this study only assessed the device on multiple handsets of the same telephone model and operating system), including a school-aged population. Reflection from smartphone

screens owing to bright sunlight can be problematic, although antiglare screens have been shown to reduce this limitation on other platforms.[25] Smartphones are on the whole more expensive than a basic Snellen chart but less expensive than a retroilluminated logMAR or Snellen chart. With the increased availability of low-cost smartphones and tablets, many health care workers may already own a device suitable for downloading multiple applications.[26]

Concerns exist about data sharing and misuse with mobile health platforms, which should be integrated with systems compliant with approved standards for data sharing.

Owing to the size, weight, and power requirements, it was not possible to perform the ETDRS chart test in participants' homes and, therefore, TRV of the ETDRS test was not assessed as with the Snellen and Peek Acuity tests. Therefore, we were unable to assess ETDRS TRV in this environment.

Nonhealth care workers who received specific training in how to use Peek Acuity performed the testing; further investigation of Peek Acuity's usability with only inbuilt instructions is required.

Testing Distance

During the early development phase, Peek Acuity was performed at 3 m. However, in the study setting, it was often not possible to find an indoor space of 3 m to conveniently perform the test. In conditions where the ambient light measure on the telephone was greater than 1000 lux, measures of Peek Acuity did not correlate well with the reference standard. With a 4.8-inch screen, 720 × 1280 pixels, and a viewing distance of 2 m, it is possible to measure acuity of 1.0 logMAR and 1.3 logMAR (Snellen equivalent of 20/200 and 20/400, respectively) when the testing distance is reduced to 1 m. Therefore, the testing distance and software algorithm were changed to 2 m. Following this change, more than 90% of participants were tested indoors in their homes. The smartphone's inbuilt ambient light detector (which was accessed in the Peek Acuity application to give a mean lux reading per VA test) provides a warning that test conditions are not suitable if more than 1000 lux is detected.

Implications

The more widespread testing of VA in low- and middle-income countries is likely to lead to greater awareness of treatable eye disease with an increased uptake of preventive and curative treatments. In nonophthalmic departments, an easily accessible, easy-to-use, accurate, and reliable vision test could lead to increased assessment of vision testing in routine practice.[27]

Conclusions

Additional applications to assess visual function and imaging of the eye make smartphones an attractive option for delivering ophthalmic assessment.[28,29] In settings where ophthalmic instrumentation or ophthalmic-trained personnel are limited, the ability to reliably measure a change in vision or detect abnormal vision, automation of stair-casing, masking of presented information, and generation of a jargon-free result greatly improve efficacy in the hands of minimally trained personnel. The inherent connectivity and global positioning system features of the device may ultimately lead to more people receiving timely and appropriate treatment.

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Study concept and design: Bastawrous, Livingstone, Jordan, Kuper, Burton.
Acquisition, analysis, or interpretation of data: Bastawrous, Rono, Weiss, Kuper, Burton.
Drafting of the manuscript: Bastawrous, Rono, Livingstone, Jordan, Burton.
Critical revision of the manuscript for important intellectual content: Bastawrous, Weiss, Kuper, Burton.
Statistical analysis: Bastawrous, Weiss.
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Study supervision: Bastawrous, Kuper, Burton.

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Original Investigation

Clinical Validation of a Smartphone-Based Adapter for Optic Disc Imaging in Kenya

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IMPORTANCE Visualization and interpretation of the optic nerve and retina are essential parts of most physical examinations.

OBJECTIVE To design and validate a smartphone-based retinal adapter enabling image capture and remote grading of the retina.

DESIGN, SETTING, AND PARTICIPANTS This validation study compared the grading of optic nerves from smartphone images with those of a digital retinal camera. Both image sets were independently graded at Moorfields Eye Hospital Reading Centre. Nested within the 6-year follow-up (January 7, 2013, to March 12, 2014) of the Nakuru Eye Disease Cohort in Kenya, 1460 adults (2920 eyes) 55 years and older were recruited consecutively from the study. A subset of 100 optic disc images from both methods were further used to validate a grading app for the optic nerves. Data analysis was performed April 7 to April 12, 2015.

MAIN OUTCOMES AND MEASURES Vertical cup-disc ratio for each test was compared in terms of agreement (Bland-Altman and weighted κ) and test-retest variability.

RESULTS A total of 2152 optic nerve images were available from both methods (also 371 from the reference camera but not the smartphone, 170 from the smartphone but not the reference camera, and 227 from neither the reference camera nor the smartphone). Bland-Altman analysis revealed a mean difference of 0.02 (95% CI, −0.21 to 0.17) and a weighted κ coefficient of 0.69 (excellent agreement). The grades of an experienced retinal photographer were compared with those of a lay photographer (no health care experience before the study), and no observable difference in image acquisition quality was found.

CONCLUSIONS AND RELEVANCE Nonclinical photographers using the low-cost smartphone adapter were able to acquire optic nerve images at a standard that enabled independent remote grading of the images comparable to those acquired using a desktop retinal camera operated by an ophthalmic assistant. The potential for task shifting and the detection of avoidable causes of blindness in the most at-risk communities makes this an attractive public health intervention.

Invited Commentary

Supplemental content at jamaophthalmology.com

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A total of 285 million people are visually impaired worldwide (Snellen acuity <6/18) of whom 39 million are blind (<3/60 better eye). Low-income countries carry approximately 90% of the burden of visual impairment, and 80% of this can be prevented or cured.[1]

There is a widening gap between the number of eye health care professionals worldwide and an increasing need as populations enlarge and age. Blinding eye disease is most prevalent in older people, and in many regions the population 60 years and older is increasing at twice the rate of the number of health care professionals.[2,3]

Diseases of the posterior segment are responsible for up to 37% of blindness in sub-Saharan Africa.[4] However, diagnosis, monitoring, and treatment are challenging in resource-poor countries because of a lack of trained personnel and the prohibitive cost of imaging equipment.

Retinal imaging is frequently used in the diagnosis and monitoring of diseases, such as diabetic retinopathy, glaucoma and age-related macular degeneration, retinopathy of prematurity,[5] and systemic diseases, such as hypertension,[6] malaria,[7] human immunodeficiency virus or AIDS,[8] and syphilis.[9]

Ophthalmologists, physicians, and eye-care workers have used ophthalmoscopes of varying types for more than 150 years, with the first reported use by Dr William Cumming in 1846.[10] The development of fundus cameras has made it possible to record and share images to collect evidence of disease presence, severity, and change.

The advent of digital imaging has made recording, processing, and sharing of images far quicker and cheaper than previous film-based methods.[11] However, retinal cameras remain impractical in many low-income countries and in primary care settings throughout the world where early detection of eye disease is prohibited because of high cost, large size, low portability, infrastructure requirements (eg, electricity and road access), and difficulty of use.

Mobile telephone access has reached near-ubiquitous levels worldwide,[12] with the highest worldwide increase in the rate of mobile telephone ownership in Africa. Telemedicine has in recent years begun to favor wireless platforms, with newer smartphone devices having high-powered computational functions, cameras, image processing, and communication capabilities.[13] Mobile telephone cameras are promising when attached to imaging devices, such as microscopes[14] and slit-lamp biomicroscopes[15]; however, they remain impractical in many remote settings because of the size and expense of the equipment to which the smartphone is attached. The development of a handheld smartphone device used in clinical microscopy has proven successful.[16]

Retinal imaging is in principle similar to using a microscope; however, it is more complex because of the interaction between the camera optics with the optics and illumination of the eye.[17] The goal of the smartphone-based adapter (Portable Eye Examination Kit [Peek Retina]) prototype was to demonstrate the feasibility of creating a portable mobile telephone retinal imaging system that is appropriate for field use in Kenya and similar contexts, characterized by portability, low cost, and ease of use by minimally trained personnel. Our primary aim was to validate such a smartphone adapter for optic nerve imaging in the context of a population-based study in Nakuru, Kenya.[18]

At a Glance

- Feasibility of a smartphone adapter for optic nerve imaging to desktop retinal camera was evaluated in Kenya.
- Differences in quality from image acquisition with a smartphone adapter by photographers not trained in health care compared with photographers trained in eye care were not identified.
- Images from the smartphone adapter appeared comparable to images from a desktop camera when independently graded by experts.
- These imaging systems may make such data collection more feasible in similar settings.

Methods

Participants

Participants included in the study were from the follow-up phase of a population-based cohort study on eye disease in Kenya (January 7, 2013, to March 12, 2014).[18] One hundred clusters were selected at the baseline (January 26, 2007, to November 11, 2008), with a probability proportional to the size of the population.[19] Households were selected within clusters using a modified compact segment sampling method.[20] Each cluster was divided into segments so that each segment included approximately 50 people 50 years or older. An eligible individual was defined as someone 50 years or older living in the household for at least 3 months in the previous year at baseline and who was found and consented to follow-up assessment 6 years later (2013-2014).

The smartphone-based adapter was available for use in the final 75 of the 100 clusters revisited, and all available participants in those clusters were examined. All participants were examined with both the smartphone-based adapter and a desktop retinal camera (CentreVue+ Digital Retinal System, Haag-Streit), which acted as the reference standard.

Ethics Approval

The study adhered to the tenets of the Declaration of Helsinki and was approved by the ethics committees of the London School of Hygiene and Tropical Medicine and the African Medical and Research Foundation, Kenya. Approval was also granted by the Rift Valley provincial medical officer and the Nakuru District medical officer for health. Approval was sought from the administrative heads in each cluster, usually the village chief.

Informed Consent

Informed consent was obtained from all participants. The objectives of the study and the examination process were explained in the local dialect to those eligible in the presence of a witness. All participants gave written (or thumbprint) consent.

Test Methods

Pharmacologic dilation in the pupils of all study participants was achieved using tropicamide, 1%, with phenylephrine, 2.5%, if

Figure 1. Examination Using the Reference Desktop Retinal Camera (A) and the Smartphone-Based Adapter (B)

needed. Dilation was not performed in participants deemed at risk for narrow angle closure (inability to visualize >180° of posterior pigmented trabecular meshwork on nonindentation gonioscopy at the slitlamp by the study ophthalmologist [A.B.][21]).

Examination with the reference camera and the smartphone-based adapter was performed in a dimly lit room; however, conditions slightly varied among clusters. An ophthalmic assistant took retinal images with the reference camera, and 1 of 2 operators or photographers used the smartphone-based adapter; all users were masked to the alternative examination. The 2 examinations took place in different rooms as availability allowed (**Figure 1**).

Reference Retinal Photography

An ophthalmic assistant digitally photographed the lens and fundus on all study participants with the reference camera, which is approved for national diabetic retinopathy screening in the United Kingdom (https://www.gov.uk/government/collections/diabetic-eye-screening-commission-and-provide). Two 45° fundus photographs were taken in each eye: one optic disc centered and the other macula centered. Images were then securely uploaded to the Moorfields Eye Hospital Reading Centre (MEHRC) for review and grading.

Smartphone-Based Photography of the Optic Disc

An experienced ophthalmic clinical officer or a lay technician with no health care background used a digital retinal camera (Samsung SIII GT-I9300; Samsung C&T Corp) and its native 8.0-megapixel camera with the smartphone-based adapter (Peek Retina) (eFigure 1 in the Supplement) to perform dilated retinal examinations on study participants. Images were recorded as video (approximate 3-10 seconds at 3-7 MB per eye) with single frames (<0.5 MB) used for disc analysis. Both examiners, henceforth termed *photographers*, received basic training in anatomy and the identification of retinal features (including optic nerve and optic cup) at the beginning of the study.

The smartphone-based adapter consists of a plastic clip that covers the telephone camera and flash (white LED) with a prism assembly. The prism deflects light from the flash to match the illumination path with the field of view of the camera to acquire images of the retina. The phone camera and clip are held in front and close to the eye, which allows the camera to capture images of the fundus.[22] A video sweep of the optic disc was performed using the adapter on a smartphone with the native camera app on each eye and securely uploaded to the MEHRC for review and grading. A 1-hour training session on how to use the smartphone-based adapter was performed before the study commenced.

In a random subset of 100 optic nerve examinations performed with the smartphone-based adapter, bespoke software (Peek Grader, Peek Vision) (**Figure 2**) was used by 2 local study examiners (one nonophthalmologist experienced in retinal examination and one with no health care training, independent of the original photographers) to select still images of the optic disc from the video sweep and use on-screen calipers to measure the vertical cup-disc ratio (VCDR) with no training provided beyond that in the app instructions on caliper placement.

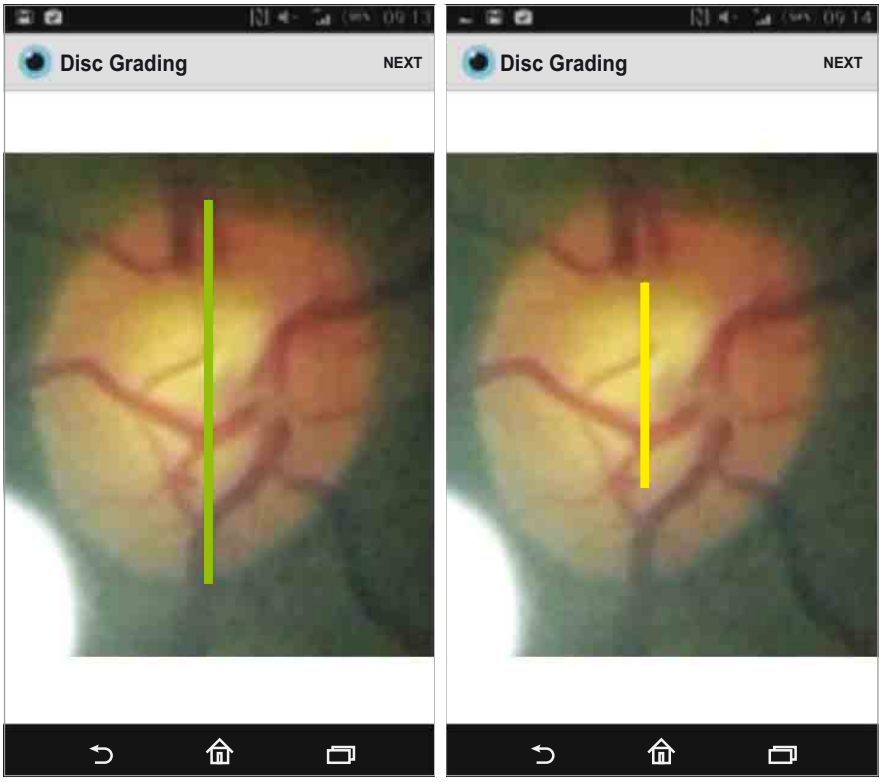
Data Management and Analysis

All images were initially examined on a large screen display for quality. For gradable images, 2 independent graders reviewed optic disc pairs. In case of grading difficulties, the adjudicator (T.P.) determined the image grade and verified a random sample of 10% of images for quality assurance and control. Graders regraded a random selection of 100 images after a minimum of 14 days to assess intragrader reliability. The adjudicator also graded 5% of randomly selected images to ensure quality control. Data were checked for consistency by a data monitor (N.S.). Optic disc images were graded as normal, suspicious, or abnormal. A disc was considered abnormal if there was neuroretinal rim thinning as defined by the ISNT rule (normal eyes have a characteristic configuration for disc rim thickness of inferior greater than or equal to superior greater than or equal to nasal greater than or equal to temporal),[23] notching or disc hemorrhage was present, or the VCDR was 0.7 or greater. A suspicious disc was one for which adjudication was necessary to determine whether its appearance was abnormal.

Service Provision

All participants identified as having treatable disease in this study were offered appropriate care, including free surgery and transport to the Rift Valley General Provincial Hospital or St Mary's Mission Hospital, Elementaita. A trained ophthalmic nurse or ophthalmic clinical officer discussed the diagnosis and

Figure 2. Peek Grader Being Used to Measure Vertical Cup-Disc Ratio on the Telephone



provided counseling to the study participants. In addition, non-study attendees were examined and treated by the study team.

Statistical Analysis

We used the Bland-Altman method[24] to analyze agreement and repeatability between and within diagnostic tests and weighted κ scores to compare the VCDR measurements made on different image sets or on regrading.[24,25] For κ weighted agreement of VCDR between observers and imaging methods, the following weights were applied: 1.0 for a 0.0 difference, 0.95 for a 0.05 difference, 0.90 for a 0.10 difference, 0.50 for a 0.15 difference, 0.20 for a 0.20 difference, and 0.00 for all differences greater than 0.20 as used in a previous analysis of disc agreement.[25] We performed the following specific comparisons:

1. Reference desktop retinal camera image repeatability: subset of 100 optic disc images randomly selected for repeat grading by an MEHRC grader to assess intraobserver agreement.
2. Smartphone-based adapter repeatability: subset of 100 optic disc images randomly selected for repeat grading by an MEHRC grader to assess intraobserver agreement (the same individuals used for reference image intraobserver repeatability assessment).
3. Reference desktop retinal camera images by expert grader on large screen vs smartphone-based adapter images using the on-screen calipers in Peek Grader (Figure 2): the same 100 images as comparisons 1 and 2.
4. Smartphone-based adapter images by an MEHRC grader on the large screen vs smartphone-based adapter images by a field ophthalmologist or layperson using Peek Grader: the same 100 images as comparisons 1 and 2.
5. Reference desktop retinal camera images by an MEHRC grader vs smartphone-based adapter images by an MEHRC grader on a large screen: all 2152 image pairs analyzed together.
6. Reference desktop retinal camera images by an MEHRC grader vs smartphone-based adapter images by an MEHRC grader on a large screen: 2152 image pairs subdivided by whether the images were collected by an experienced photographer or a lay photographer.

Results

Participants

Recruitment took place from January 7, 2013, to March 12, 2014. A total of 1460 individuals from 75 clusters participated. Their mean (SD) age was 68 (9) years (range, 55-99 years), and 700 (47.9%) were female. Participants underwent retinal examination using the smartphone-based adapter and the standard desktop retinal camera. A total of 2920 eyes were imaged, of which 2152 eyes (73.7%) had gradable images from both the smartphone-based adapter and the reference camera. In 170 eyes, a gradable image was obtainable with the smartphone-based adapter but not the reference camera, and, conversely, in 371 eyes, a gradable image was obtainable with the reference camera but not with the smartphone-based adapter. In 227 eyes a disc image was not possible from either modality (eFigure 2 in the Supplement).

Table. Agreement (Bland-Altman and Weighted κ) of Optic Disc VCDR Scores Among Different Imaging Modalities and Different Graders[a]

Comparison No.[b]	Reference Image			Comparison Image			No. of Eyes	Mean VCDR Difference (95% CI)	Weighted κ, Mean (SD)
	Camera	Grader	Screen	Camera	Grader	Screen			
1	Reference camera	Expert	Large	Reference camera	Expert	Large	100	−0.07 (−0.21 to 0.07)	0.90 (0.01)
2	Smartphone	Expert	Large	Smartphone	Expert	Large	100	−0.01 (−0.18 to 0.16)	0.77 (0.04)
3a	Reference camera	Expert	Large	Smartphone	Ophthalmologist	Telephone	100	−0.08 (−0.11 to −0.53)	0.30 (0.07)
3b	Reference camera	Expert	Large	Smartphone	Nonophthalmologist	Telephone	100	−0.07 (−0.38 to 0.24)	0.19 (0.06)
4a	Smartphone	Expert	Large	Smartphone	Ophthalmologist	Telephone	100	−0.08 (−0.11 to −0.56)	0.35 (0.07)
4b	Smartphone	Expert	Large	Smartphone	Nonophthalmologist	Telephone	100	−0.06 (−0.33 to 0.21)	0.25 (0.06)
5	Reference camera	Expert	Large	Smartphone	Expert	Large	2152	0.02 (−0.21 to 0.17)	0.69 (0.01)
6a	Reference camera	Expert	Large	Smartphone (experienced examiner)	Expert	Large	1239	−0.02 (−0.20 to 0.17)	0.68 (0.02)
6b	Reference camera	Expert	Large	Peek (lay examiner)	Expert	Large	913	−0.02 (−0.21 to 0.16)	0.71 (0.02)

Abbreviation: VCDR, vertical cup-disc ratio.

[a] Expert indicates grading was performed by an independent trained grader or image reader; nonophthalmologist, grading performed by a non–health care worker; and ophthalmologist, grading performed by an ophthalmologist.

[b] The comparison number relates to the specific comparisons that are described in the Methods section.

Reference Image Disc Parameters

The VCDR parameters derived from the analysis of the 2152 reference desktop retinal camera images from this population (eFigure 3 in the Supplement), using the definitions in the International Society for Geographical and Epidemiological Ophthalmology classification, were as follows: mean VCDR, 0.38; 97.5th percentile VCDR, 0.7; and 99.5th percentile, VCDR 0.9.

Intraobserver Repeatability

A set of images from 100 eyes were used to assess intraobserver repeatability. Bland-Altman analysis and κ scores found excellent intraobserver repeatability for the MEHRC graders for both the reference desktop retinal camera images (**Table**, comparison 1) and the smartphone-based adapter images (Table, comparison 2).

Comparison of Expert and Field Grading

For the same 100 eyes, we compared the VCDR measured on the reference desktop retinal camera images by the MEHRC grader and the images of the same eye taken with the smartphone-based adapter with the VCDR graded on the telephone screen (Figure 2) by an ophthalmologist (Table, comparison 3a) or a layperson (Table, comparison 3b). Although the mean difference of the mean by the Bland-Altman method was less than 0.1, the weighted κ scores were relatively low. We performed a similar analysis with the smartphone-based adapter image graded by the MEHRC grader compared with the VCDR measured with the Peek Grader (Table, comparisons 4a and 4b). We again found a small difference in the mean difference but low κ scores.

Comparison of Reference and Smartphone-Based Adapter Images

We compared (Table, comparison 5) the VCDR measured by an expert grader (MEHRC) from the smartphone-based adapter and reference digital retinal camera images for 2152 eyes (eTable in the Supplement). The Bland-Altman analysis found a difference in the mean of −0.02 (95% CI, −0.21 to 0.17) (**Figure 3**).

Interexaminer Variability

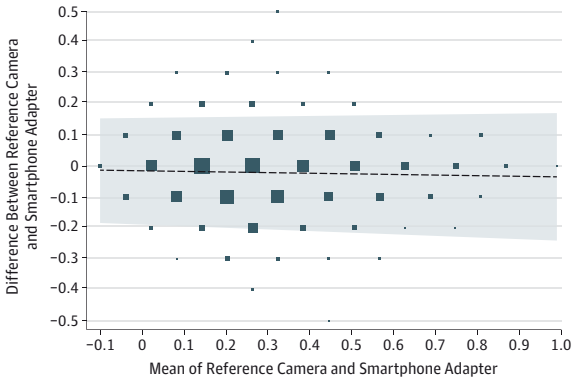
Two members of the field team collected retinal images using the smartphone-based adapter. The first was a trained eye care worker experienced in the assessment of the retina (experienced photographer). The second had no prior health care or eye care experience but was proficient in the use of a smartphone (lay photographer). Bland-Altman analysis was performed comparing the reference images and smartphone-based adapter images, both graded at the MEHRC. For the 1239 eyes that had smartphone-based adapter images collected by the experienced retinal photographer, the difference in the mean was −0.02 (95% CI, −0.22 to 0.17) (Table, comparison 6a). For the 913 eyes that had smartphone-based adapter images collected by the lay photographer, the difference in the mean was also −0.02 (95% CI, −0.20 to 0.16) (Table, comparison 6b). There was no observable difference in image acquisition quality between the experienced retinal photographer and lay photographer.

Discussion

The findings of this study are discussed within the context of optic disc imaging in a population-based study in Kenya. We compared the performance of 2 imaging modalities and different image-grading expertise. The results indicate that smartphone-based adapter images, when analyzed by an independent expert, have excellent agreement with images from a reference desktop retinal camera read by the same expert.

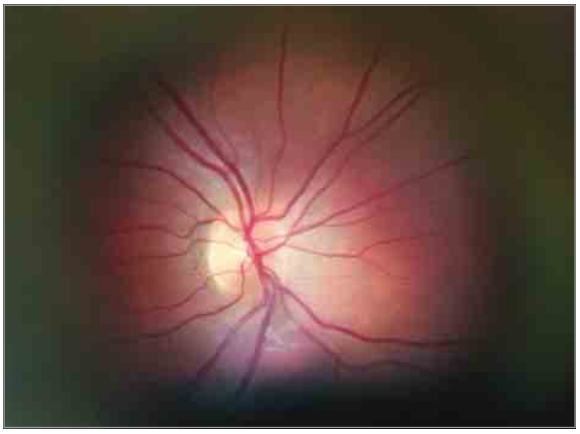
Intraobserver agreement within imaging modalities was also excellent for the reference camera and the smartphone-based adapter images. This finding indicates a high degree of confidence to be able to measure real change over time when a threshold for VCDR increase of 0.2 or greater is used.

Figure 3. Bland-Altman Plot of 2152 Optic Nerve Images Taken From the Reference Desktop Retinal Camera and the Smartphone-Based Adapter



Both images were graded by an expert grader at Moorfields Eye Hospital Reading Centre.

Figure 4. Retinal and Optic Disc Image From Peek Retina Mark VI Taken Through a Dilated Pupil With an Approximate Field of View of 20° to 30°



Although the Bland-Altman limits of agreement were acceptable for all comparisons, the smartphone-based adapter, particularly when performed by a nonclinically trained user, was of only fair or slight agreement with the expertly graded reference image. The lower levels of agreement with the smartphone-based adapter may be accounted for by images being graded on a small screen with no user guidance given beyond basic instructions within the app to "measure the disc" and "measure the cup."

Although stereoscopic disc images are the preference for optic nerve grading, monoscopic images, as used in this study, do not represent a disadvantage for grading glaucoma likelihood.[26] The finding that nonclinically trained personnel can acquire images of the optic disc using a low-cost smartphone adapter that are of a standard that appears comparable to a desktop retinal camera operated by a dedicated ophthalmic technician or assistant suggests there is potential for use of such devices in mobile health and tele-ophthalmology.

In this study, we only assessed optic disc features; however, potential use in retinal diseases warrants further investigation, the findings of which would have implications for diabetic retinopathy screening programs. Previously described uses of smartphone-based cameras for diabetic retinopathy have been in a clinic setting when operated by a retinal specialist and found to provide good agreement with slitlamp biomicroscopy examination also performed by a retinal specialist.[27,28] Further assessment of smartphone-based tools by nonspecialists in nonophthalmic settings is warranted.

A limitation of this study, typical of clinical research based on highly iterative technologies, is that, in relying on rapidly evolving platforms, the time to dissemination of results is long compared with the evolution of the technology itself. This limitation often results in the presentation of data from technology that have been superseded by subsequent prototypes or commercially available devices. In this field study, an early iteration of the smartphone-based adapter (internally identified as mark II) was used throughout. However, by the time of completing the analysis, a more advanced iteration of the smartphone-based adapter (mark VI) was available. An image acquired using mark VI is shown in **Figure 4**. When compared with Figure 2, which shows an image from mark II, a significant improvement is evident.

A further limitation is that no evaluation of optic discs from either imaging modality was performed without mydriasis. Previous investigations have found the limits of agreements between nonmydriatic optic disc grading to be outside clinically acceptable levels.[29] We found it possible to acquire good optic nerve images in undilated pupils of 2.5- to 3.0-mm diameter.

The smartphone-based adapter prototypes, subsequent commercially available devices, and alternative portable retinal imaging systems could contribute to tackling avoidable blindness and in screening for diseases with eye manifestations, particularly in low-income countries and remote communities where mobile telephone infrastructure is ubiquitous but trained personnel are few. Existing telecommunications infrastructure can enable greater access to health care by permitting timely diagnosis using data sharing via the communication capabilities intrinsic to the telephone. With the development of automated retinal imaging systems,[30] we could see real-time diagnostics by a technician rather than by the more scarcely available eye care personnel.

Coupling imaging with other smartphone-based diagnostic tests[31] and geotagging enables database creation of examined individuals based on predetermined parameters as demonstrated by systems such as EpiCollect.[32] Such systems make follow-up and epidemiologic data collection more feasible in resource-poor settings.

Conclusions

Smartphone penetration continues to increase with higher computing power, purpose-built software and hardware, greater connectivity, and lower handset costs. There is now an opportunity to reach the most underserved populations in a manner that was not possible just a decade ago.

ARTICLE INFORMATION

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Author Contributions: Dr Bastawrous had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
Study concept and design: Bastawrous, Shah, Kuper, Burton.
Acquisition, analysis, or interpretation of data: All authors.
Drafting of the manuscript: Bastawrous, Shah, Livingstone, Hu.
Critical revision of the manuscript for important intellectual content: Bastawrous, Giardini, Bolster, Peto, Livingstone, Weiss, Rono, Kuper, Burton.
Statistical analysis: Bastawrous, Peto, Weiss, Hu.
Obtained funding: Bastawrous, Burton.
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Original Paper

Analysis of Eye Care Services in Kenya and the Acceptability, Usability, and Views on Deployment of Peek, a Mobile Phone mHealth Intervention for Eye Care: A Qualitative Study

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Abstract

Background: The Portable Eye Examination Kit (Peek) is a mobile phone–based ophthalmic testing system that has been developed to perform comprehensive eye examinations. Peek offers a solution for overcoming barriers of limited access to traditional ophthalmic testing methods and has been pilot tested on adults in Nakuru, Kenya, and compared with traditional eye examination tools. Shortages in ophthalmic personnel, the high cost, and the difficulty in transporting equipment have made it challenging to offer services, particularly in rural areas.

Objective: This qualitative study evaluated the acceptability and usability of Peek in addition to perceptions regarding its adoption and nationwide deployment.

Methods: Semistructured interviews were conducted and analyzed using a framework approach. This included analysis of interviews from 20 patients, 8 health care providers (HCPs), and 4 key decision makers in ophthalmic health care provision in Kenya. The participants were purposefully sampled. The coding structure involved predefined themes for assessing the following: (1) the context, that is, environment, user, task, and technology; (2) patient acceptability, that is, patients' perceived benefits, patient preference, and patient satisfaction; (3) usability, that is, efficiency, effectiveness, learnability, and flexibility and operability of Peek; and (4) the benefits of Peek in strengthening eye care provision, that is, capabilities enhancer, opportunity creator, social enabler, and knowledge generator. Emerging themes relating to the objectives were explored from the data using thematic analysis.

Results: Patients found Peek to be acceptable because of its benefits in overcoming the barriers to accessing ophthalmic services. Most thought it to be fast, convenient, and able to reach a large population. All patients expressed being satisfied with Peek. The HCPs perceived it to satisfy the criteria for usability and found Peek to be acceptable based on the technology acceptance model. Peek was also found to have features required for strengthening ophthalmic delivery by aiding detection and diagnosis, provision of decision support, improving communication between provider and patient and among providers, linking patients to services, monitoring, and assisting in education and training. Some of the deployment-related issues included the need for government and community involvement, communication and awareness creation, data protection, infrastructure development including capacity creation, and training and maintenance support.

Conclusions: According to all parties interviewed, Peek is an acceptable solution, as it provides a beneficial service, supports patients' needs, and fulfills HCPs' roles, overall contributing to strengthening eye health.

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KEYWORDS

mobile phone; mHealth; qualitative; ophthalmic testing; acceptability; usability

Introduction

Background

The estimated number of visually impaired people worldwide is 285 million, of which 39 million are blind [1]. Up to 80% of global visual impairment is preventable [1].The burden is unequally distributed, with the largest proportion living in low-income nations of Africa and Asia [2]. Loss of sight is associated with considerable emotional, social, and economic consequences, especially among the poor [3,4]. One of the biggest challenges to reducing the burden of visual impairment is the significant shortage of ophthalmic health care [5]. Ophthalmic testing equipment is often expensive, bulky, and immobile, making it difficult to deploy an ophthalmic service in rural areas, particularly where there are fewer ophthalmic professionals.

Tackling avoidable vision loss requires strengthening of health systems (HSs) in order to achieve universal access to ophthalmic services. This has been a major focus of the global ophthalmic public health community and a key goal of the recent World Health Organization (WHO) global action to improve eye health for everyone over the next 5 years, building on the principles of VISION 2020 [6].

Mobile health (mHealth) refers to the use of mobile technology, such as mobile phones (MPs), to provide health services. Mobile health is a growing field and its potential in improving health and health care delivery has been well demonstrated [7-9]. There are significant opportunities to leverage the benefits of mHealth in expanding health care delivery with the increasing uptake of MPs in the developing world [10]. Furthermore, the scope of mHealth has increased in recent years with the introduction of smartphones, which offer enhanced functionality and user interfaces over traditional multimedia devices.

In Africa, smartphones are becoming more affordable, driven by greater competition among operators and manufacturers. Smartphone subscriptions in Africa have been forecast to increase from 79 million to 412 million between 2012 and 2018 [11]. Nevertheless, the evidence base for smartphone use in health care is lacking, particularly contextual process and health outcome evaluations in low- and middle-income countries [12-16].

This study aimed to evaluate a smartphone-based ophthalmic examination system with clip-on hardware, the Portable Eye Examination Kit (Peek), which has been developed and introduced as a user-friendly and affordable alternative to perform comprehensive ophthalmic examinations. Peek offers a potential solution to overcoming barriers of traditional ophthalmic testing methods and thereby contributes to the VISION 2020 goals [17].

Objectives

This qualitative study was carried out to assess patients', health care providers' (HCPs'), and stakeholders' (decision makers in ophthalmic service provision are referred to as "stakeholders") perspectives on the adoption of Peek for improving the provision of ophthalmic services in Kenya. This included a formative evaluation of the acceptability and usability of Peek compared with traditional methods of ophthalmic testing. In addition, its potential for strengthening ophthalmic services and potential barriers and facilitators to adoption and deployment of the technology were explored.

Methods

This study was undertaken within the follow-up phase of the Nakuru Eye Disease Cohort Study in central Kenya, a population-based study, which recruited 5000 individuals from 100 clusters [18].

The sampling strategy for this qualitative study involved purposeful sampling, and the patient sample was chosen from the 100 clusters based on varying sex, age, geographical location, educational levels, and income. The purpose was to maximize diversity and capture common themes relating to the intervention across a range of participants with differing characteristics [19]. Nakuru district was chosen because it offers a diverse population in terms of ethnicity and economic activities [18].

The qualitative study consisted of semistructured interviews with all HCPs (ie, 8) recruited for testing Peek, patients (ie, 40) examined with Peek, and key stakeholders (ie, 4) involved in shaping ophthalmic provision in Kenya and were chosen from the ministry of health, an ophthalmic teaching hospital, and selected nongovernmental organizations (NGOs). All patients underwent visual acuity (VA) testing using Peek at their homes, whereas fundal images were taken at a temporary clinic in that cluster. At this clinic, they also underwent repeat VA and funduscopic examinations using traditional equipment.

Four interviewers were trained to conduct the interviews and were provided semistructured interview guides. All interviews were audio recorded with the consent of all participants. The patient interviews were conducted in Kiswahili and then transcribed and translated. Conversely, the HCP and stakeholder interviews were conducted in English.

The Nakuru Eye Disease Cohort Study was approved by the African Medical and Research Foundation ethics board, which included pilot testing of Peek and conducting interviews as part of the larger project. Full written consent was obtained from all parties including the patients, HCPs, and stakeholders before each interview and was available in Kiswahili and English.

The interview transcripts were analyzed using NVivo version 10 [20]. A framework analysis approach was used, creating predefined themes for the coding structure. The coding framework was guided by theoretical constructs from literature on mobile usability, acceptability of technology, and previous mHealth reviews and literature on assessing benefits of mHealth in strengthening health care delivery [21-34].

To assess the acceptability and usability of Peek, it was deemed important to first understand the context within which it is to be implemented [21-23]. The analysis of the context was therefore carried out through a coding framework proposed by a qualitative review of mobile usability studies, which took into account the environment, user, task, and technology [21]. The themes involved assessing patients' and HCPs' perceptions of (1) ophthalmic service provision; (2) the barriers to seeking and accessing ophthalmic services, that is, environment; (3) HCP role and experience, that is, user; (4) understanding the purpose of Peek, that is, task; and (5) familiarity and views regarding mobile technology.

The coding for assessing patient acceptability of the Peek testing process and its functionality was informed by the definition of acceptability by Ayala and Elder (2011) [24]. They proposed that acceptability refers to determining how well an intervention will be received by the target population and the extent to which the new intervention or its components meet the needs of the target population and organizational setting. The themes included assessing (1) patients' perceived benefits of Peek, (2) patient satisfaction, and (3) patient preference.

The International Organization for Standardization defines usability as the extent to which a product can be used by specific users to achieve specific goals with efficiency, effectiveness, and satisfaction in a specified context of use [25]. A number of usability dimensions have been proposed by Coursaris and Kim (2006) in their qualitative review of mobile usability studies, which informed the coding framework for assessing usability of Peek by HCPs [21]. The themes included (1) efficiency, (2) effectiveness, (3) learnability, and (4) flexibility and operability.

The Technology Acceptance Model (TAM) and its extension, TAM2, were used as a guide to assess user acceptability of the technology [26-29]. This proposes that acceptability or prediction of use of a technology depends on the attitude toward it, which is a function of ease of use and perceived usefulness. The analysis of perceived usefulness was informed by assessing HCPs' perceptions of the benefits. Several studies to date have looked at the benefits of mHealth, and several frameworks have been proposed for assessing benefits in strengthening health care provision [30]. This analysis has therefore adapted a model based on a combination of four frameworks to appraise the potential benefits of Peek in strengthening eye care delivery. The four main themes of the framework were adapted from the Information Communication Technology for Healthcare Development Model [31]. These are capabilities enhancer, social enabler, opportunity producer, and knowledge generator. The subthemes were based on three other frameworks proposed for guiding assessment of mHealth in strengthening HSs [9,30,32,33]. The components chosen for the framework are also in line with the categories of mHealth initiatives established by the WHO [34].

A thematic analysis was also conducted to explore emerging themes and subthemes related to the study objectives that were inferred from the data [35-37]. Analysis was conducted until saturation was reached, which was 20 patient interviews, all 8 HCP interviews, and all 4 stakeholder interviews. After this, the coding was summarized and modified, and connections were made between related themes and between the 3 groups of interview participants.

Results

A summary of all the themes discussed in this section is given in Textbox 1.

Textbox 1. Results section summary.

Contextual factors

- Environment
- Patient demographics
- Barriers to seeking and accessing services
- Cost
- Lack of ophthalmic facilities, qualified providers, and support
- Time
- Lack of awareness
- User
- Role and experience of health care providers
- Task
- Patient's and health care provider's understanding of Portable Eye Examination Kit
- Technology
- Attitudes toward mobile phones

Patient acceptability

- Perceived benefits of Portable Eye Examination Kit
- Patient preference
- Patient satisfaction

Usability dimensions

- Efficiency
- Time
- Multitasking
- Portability and convenience
- Cost
- Effectiveness
- Learnability
- Flexibility and operability

Benefits

- Capabilities enhancer
- Detection and diagnosis
- Provider performance
- Decision support
- Social enabler
- Provider-to-patient communication
- Provider-to-provider communication
- Opportunity producer
- Linkage of patients to ophthalmic provision
- Monitoring and surveillance
- Knowledge generator
- Training and education

Contextual Factors

Patient Demographics

The number of males and females was equal and the ages of the patients ranged from 50 to 77 years. The educational levels varied from no education to primary, secondary, and tertiary education and were evenly represented in the sample of patients. With regard to occupation, 11 patients were farmers, 2 teachers, 2 businessmen or businesswomen, an engineer, an industrial chemist, a civil servant, and a secretary. Apart from one businessman who reported an annual income of 4,000,000 Kenyan shillings (KES), incomes varied mainly from 1000 to 50,000 KES per month with an average of 16,000 KES.

Environment (Patients' and HCPs' Perceptions of Current Eye Service Provision and Perceived Barriers to Seeking and Accessing Eye Services)

Cost

Six of the HCPs and almost all patients stated seeking ophthalmic services as unaffordable when referring to having to pay for hospital bills and transport.

> *...seeking eye treatment is quite expensive. Then again, I was not in a position to seek treatment. As farmers, we have low standards of living and therefore cannot afford to seek regular eye healthcare. We only go to hospitals when eye problems persist.* [Patient #23, male]

Lack of Ophthalmic Facilities, Qualified Personnel, and Support

The general opinion among the HCPs was that the availability of eye services in Kenya was inconsistent, with poorer provision in rural areas. The majority mentioned that patients had to travel long distances to access eye care, which was made more difficult because of poor infrastructure and roads. Another issue raised was scarcity of qualified ophthalmic personnel. Many described existing services as being overburdened as a result. With regard to prevention, most HCPs reported that they were not aware of any formal preventive measures put in place by the government in the region studied. The majority mentioned often taking the initiative to educate patients when seeing them.

Similarly, from patients' point of view, the government services in rural areas were reported to be limited to dispensaries with no specialist ophthalmic testing services, which only provide eye medications at a cost. Most patients also mentioned being on their own with little support posing a challenge for them to access treatment either because of the inability to access transport or due to having to prioritize other issues to sustain their livelihood. All those living in remote settings stated they were constrained from accessing more specialist services because of long distances.

In contrast, those living in Nakuru, an urban town, felt that ophthalmic facilities were generally accessible via government hospitals, private hospitals, opticians, and missionary hospitals.

> *Most patients are very far from health facilities, we have poor infrastructure and most clinics, health facilities that are near people don't have eye clinic specialist, they just have a general doctor or clinician and that is all. So you find that most patients don't get specific eye treatment.* [HCP #6, female]

> *It is far and then again, it is not easy to find. It is hard because even fare has to be considered and on top of that, there is the fee for treatment which is steep.* [Patient #2, female]

Time

Time was reported as a significant barrier to accessing eye services by 4 HCPs. Patients also had a similar opinion, especially those living in urban settings where long queues at government facilities were reported as a major obstacle because of difficulty taking time off work and potential loss of income.

> *Transportation and also long queues, time is also a factor because some are trying to work hard to see how the family could get along so they say the issue of the eye can be put aside, although he cannot see properly he says it's an issue he can attend to later.* [Patient #39, male]

Lack of Awareness

Six HCPs mentioned lack of knowledge of eye conditions and lack of awareness of the importance of early detection and treatment as a barrier to patients seeking health care in both rural and urban settings. However, they perceived this to be more of a problem in rural areas due to lower educational levels and less exposure to health care in general.

Patients acknowledged that they had limited knowledge of eye problems. Most patients gave similar explanations for causes of eye problems and demonstrated a particularly limited understanding of chronic conditions. The most frequently mentioned causes, as perceived by patients, were poor hygiene, dust, smoke from cooking, direct sunlight, and unbalanced diet. A couple of participants mentioned "jerreri" as a cause, which means cataracts in their local language. Few patients mentioned other causes such as inherited diseases, work, alcohol, and smoking.

Interestingly, most patients revealed that they did not see the importance of regular eye checks despite being affected by changes in their vision. Only 4 patients brought up the importance of timely eye checkups as a means of preventing visual deterioration.

When asked about delays in seeking treatment, the most common reason given by patients and HCPs was that eye problems were not perceived to be serious enough to require urgent treatment, particularly when faced with barriers to accessing services. Furthermore, patients and HCPs perceived local myths and traditional practices in their communities to be a consequence of poor knowledge, leading to patients not seeking or accepting treatment. They highlighted the need for awareness creation through education and involvement of village chiefs.

> *...I thought that the problem was not very serious and I waited to see whether I would get better on my own but when that did not work, I sought medical treatment. This is because there are no mobile eye*

> *doctors like you doing rounds creating awareness on eye issues. Someone like I will wait until I am sick to seek treatment because there is no one giving people information to help prevent these problems*. [Patient #9, male]
>
> *They should receive help from people like chiefs who are more knowledgeable. They should be helped in accessing treatment. It can help in prevention. Because most people are now useless*. [Patient #2, female]

User (Role and Experience of Health Care Providers)

There were 6 male and 2 female HCPs consisting of ophthalmologists, ophthalmic clinical officers, and members of the advance team. The members of the "advance team" were responsible for tracking participants for the study enumeration, using Peek to test vision at patients' home and ophthalmic testing using traditional equipment in clinics. One of them had the additional responsibility of software maintenance. An ophthalmic nurse was also part of this team and was also involved in counseling and preparing patients for surgery. Most HCPs had no prior training in eye care before joining the Nakuru Eye Disease Cohort Study. Their experience in ophthalmic service provision was therefore mainly limited to the year during which the study took place, with the exception of the ophthalmologists, one of whom had 18 months and the other 4 years of experience.

Task (Understanding of Peek)

When asked to describe Peek and the examination process, the responses from HCPs varied based on their role and experience as ophthalmic providers. Most HCPs correctly mentioned that Peek incorporates several examinations in one device, thus enabling a basic eye examination comparable to traditional techniques. All the HCPs who were primarily responsible for providing outreach services described Peek as a tool for VA testing, and most needed prompting before mentioning its other uses in performing eye examinations such as anterior eye examination and fundoscopy. Most HCPs also highlighted Peek's capability for data analysis, information sharing, communication with colleagues, and other basic functionalities such as browsing, testing, and calling.

The patients interviewed demonstrated a good understanding of the technology and its purpose for ophthalmic testing and described it as an alternative and possible substitute for traditional eye examination. Two patients, however, were not aware that the MP was being used for eye examinations.

Technology (Attitudes Toward Mobile Phone Technology)

Patients, HCPs, and stakeholders all had positive attitudes toward MPs and smartphone technology. Mobile phones were referred to as innovative, advanced, new, and highly technological. They reported that the technology had made communication easier. Several patients revealed a familiarity in using MPs and felt that the attitude of the community toward MPs depends on exposure, awareness, and education. The HCPs and stakeholders had similar views and mentioned that MP use was widespread in the area. One HCP and patient reported that the use of MPs in Kenya was best known by the money transfer initiative called M-Pesa that has been adopted by a large proportion of the population. All participants were optimistic about the potential uses of MPs, especially smartphones, and portrayed enthusiasm for technology.

> *I think that the MP is a highly technological piece of equipment. It is very advanced*. [Patient #27, female]
>
> *In Kenya generally people are used to SMS, they are used to M-Pesa and the technology which is there is almost comparable to that. I think the kit generally most people are able to operate*. [HCP #3, male]
>
> *We all like new technology, we are all thirsty for new innovations in eye health because of the many challenges in service delivery*. [Stakeholder #4]

Patient Acceptability

Benefits as Perceived by Patients

All patients perceived Peek to be beneficial as its portability brings examination and treatment closer to them. They perceived it as a way of overcoming many of the aforementioned barriers. The patients also suggested that it could increase detection of eye problems because it can reach a larger population. This could be achieved by providing earlier eye examinations for those who lack awareness or those unable to access existing eye services. The use of Peek was also seen to have the potential to increase awareness about eye conditions in general as it uses mobile technology, which is considered to be acceptable for patients. Many patients also deemed Peek to be efficient and economical for themselves and the HS because it saves time, costs less, and reduces the burden on health care personnel. When patients were asked about how long it took to receive an eye examination with Peek, 17 of the 20 patients recalled the time to be between 2 and 20 minutes. The other 3 patients did not mention an exact time. When they were asked about the duration of traditional eye examinations, the responses varied between 30 minutes and 4 hours.

Patient Satisfaction

All patients stated that they were satisfied with the service offered. Eighteen of 20 patients did not report concerns regarding the technology. Moreover, when asked about further comments about Peek at the end of the interview, the majority of patients stated that they were hoping for the service to be more accessible to them.

Nevertheless, some patients expressed potential doubts about their community's uptake of Peek. These will be discussed later in this paper.

Patient Preference

When asked about whether patients preferred traditional examinations or Peek, 10 patients expressed a preference for Peek, 7 stated no preference, and 3 preferred the traditional examination. The main reasons for preferring Peek were shorter examination time, simplicity, efficiency due to multiple examinations combined in one tool, being seen at home, and the increased potential coverage of the population in need. Those who did not express a preference stated that their decision would

be dependent on the actual availability of the intervention. Two patients who preferred traditional examinations referred to the ease of reading larger letters. Another patient described clinic equipment as having fewer potential side effects, although he then conveyed his support for Peek to be incorporated into policy service provision in rural areas where the need was perceived to be greatest.

Patient Acceptability as Perceived by Health Care Providers

The HCPs also perceived Peek to be acceptable to patients. They reported that patients appreciate a service that is brought closer. Furthermore, according to HCPs patients were curious, interested, and willing to be examined by the new technology. Some HCPs also mentioned that the use of Peek helped overcome patients' fears related to being tested with traditional techniques, as mobiles are more familiar and therefore patients are likely to be more comfortable being tested with MPs.

> *The application being the first to debut in Kenya mostly using testing people with it, it is amazing and people are like they wish to be checked using the phone*. [HCP #4, male]

Analysis of Health Care Providers' Usability of Peek

Usability Dimensions

Bearing in mind the context of use described earlier, an analysis of usability was carried out using the predefined usability dimensions, that is, efficiency, effectiveness, learnability, and flexibility and operability, as summarized in Table 1. While assessing efficiency, the following subthemes became apparent: speed, multitasking, convenience, and cost. Table 1 summarizes the analysis of perceptions of the HCPs regarding usability of Peek as per predefined usability dimensions.

Table 1. Usability dimensions.

Usability dimension		No. of HCPs[a]	Rationale given by HCPs	Benefits relating to usability dimension	HCP quotes
Efficiency					
	Time	8	Simple and easy to use, with less manual record keeping.	Ability to see more patients, early diagnosis, and treatment.	"*...it will be more effective in that we will be able to get to see more patients with eye problems and in that case I will be able to solve them early enough and our patients will not have to go blind...*"
	Multitasking	6	Requires less equipment to navigate and manpower to conduct examinations.	Saves human resources.	"*...you can multi task it by doing all the examination at the same place without moving just by the touch of the application, so it will make it better.*"
	Portability and convenience	7	Easier to carry around compared with traditional equipment.	Increase access and coverage in remote areas.	"*...it's portable and one can be able to access rural areas where infrastructure is poor so in terms of accessing those places you will be able to get people who could not think of getting help...*"
	Cost	6	Cheaper equipment (10,000-40,000 KES[a] compared with more than 1,000,000 KES for traditional equipment), transport, and negligible software costs and replacement costs.	Economic gains for patients and service provisions.	"*...the cost of one Portable eye kit does like very many examination procedures compared to the machines so it makes it cheaper, two the cost of transport is cut down because I'll be able to visit the client at his/her own convenience...*"
Effectiveness		6	Accurate, equal, or better than traditional equipment.	Ability to provide better analysis of findings, compared with the substitute.	"*The phone is automatically accurate than the traditional type of equipment. PEEK is more advanced than the traditional equipment gives you the exact figures and images. It is very accurate. Excellent in fact*"
Learnability		8	Clear instructions; though useful, no expertise required.	Usable by less qualified HCPs with limited smartphone knowledge.	"*...anybody as long as you have something in between your ears that is a brain then you can actually work. Because everything is just written and where it is not written you can actually see it everything is self-explanatory with algorithms.*"
Flexibility and operability		8	Quickly modifiable based on user feedback and robust technology.	User-friendly, easy to maintain, and meets different needs.	"*...it is still open ended it is not closed so it is it is able to accommodate, new things and new ideas and new situations that may vary from one region to another from one country to another so it is adaptable.*"

[a] HCP: health care provider; KES: Kenyan shilling.

HCPs' and Stakeholders' Perceptions of Benefits of Peek in Eye Care Delivery Using a HSs Approach

Capabilities Enhancer

Detection and Diagnosis

The HCPs and stakeholders believed that Peek can increase the chances of diagnosing eye problems and is thought to have the potential to be used as a screening tool to increase detection of poor vision. They perceived earlier detection to be beneficial in reducing the burden of blinding eye disease and thereby increasing general standards of living. Nevertheless, stakeholders stated that the success of Peek as a screening tool will depend on proven accuracy, sensitivity, availability, and ensuring high-quality service delivery.

> *Well the more sensitize a technology you have for detecting problems and the more easily available it is, it means you are going to start detecting many more patients and so that's good for the patients so that more people get to know more earlier that they have a problem*. [Stakeholder #1]

Provider Performance and Decision Support

The opinion among HCPs and stakeholders was that Peek could allow for task shifting and improved human resource management by providing support to community health volunteers (CHVs). This was seen as a potential solution to fill in for the shortage of ophthalmic workforce. Peek was perceived to lead to improved outcomes of the services provided as a direct result from its user-friendly platform, inbuilt decision-support algorithms, and data analysis capabilities. These features of the application were also perceived to help in managing and organizing workload of HCPs, for example, by prioritizing referrals. Furthermore, the application was thought to have an impact on increasing HCP motivation and self-confidence in detecting and consequently managing eye problems.

> *I can even be able to collect, gather data from the field and it gives me some clear information on some decisions that I am about to make. The same way the smartphone and for example PEEK is doing; it is able to do some basic examination that is able to separate those who need to see a doctor urgently and those who do not need urgently*. [Stakeholder #3]

Social Enabler

Provider-to-Patient Communication or Client Education

Most stakeholders stated the value of Peek in providing instant feedback to patients through the images, which are immediately available on the phone. Stakeholders described its value in terms of explaining the diagnosis to the patient, reinforcing patient understanding, decision-making, and confidence. According to one stakeholder, this is further enhanced by the ability to contact relatives who are unable to make it to the clinic. Stakeholders highlighted that seeing an image of a damaged retina and optic nerve can help patients understand the seriousness of their problem and thus they will be more likely to urgently seek and comply with treatment as a result.

Provider-to-Provider Communication

Stakeholders referred to the potential role of Peek in enhancing communication between HCPs as a beneficial feature, for example, enabling remotely located ophthalmologists to provide less qualified HCPs with support in decision-making. Peek was also perceived to overcome current problems in data transfer by generating images in a format that can easily be transferred to other HCPs, which existing equipment does not allow. These qualities of Peek are further reported as vital for task shifting to be successful.

Opportunity Producer

Linkage of Patients to Ophthalmic Provision

Similar to HCP views, according to all the stakeholders interviewed, Peek was perceived as bringing service provision closer to patients who need it most. This was deemed possible by being able to conveniently and efficiently provide ophthalmic services in remote settings, thereby overcoming logistical issues in having to set up clinics. Additionally, 2 stakeholders commented on the ability of Peek to increase public confidence in ophthalmic workers and in service provision, which is currently challenged by poor uptake of eye services.

> *...those who are in the most remote areas who have the highest prevalence for blindness will now be linked to the health system and so people will be able to find them and treat them*. [HCP #7, male]

Monitoring and Surveillance

Features of Peek such as data storage and Global Positioning System tracking are thought to be desirable by stakeholders in strengthening monitoring and surveillance, thereby better contributing to policy-making and resource planning. Additionally, they perceive Peek to enhance follow-up by being able to locate patients easily.

Knowledge Generator

Training and Education

Peek was also deemed as a training opportunity by both HCPs and stakeholders, because discussing management of eye problems with qualified and experienced ophthalmic professionals is thought to increase knowledge and skills of those with limited training. Furthermore, according to stakeholders and HCPs, Peek offers an opportunity to educate and sensitize the population about eye health. Consequently, the overall opinion was that Peek contributes to increased patient awareness and knowledge.

Analysis of Perceived Barriers, and Proposed Facilitators for Overcoming Potential Barriers to Adoption and Deployment

Neither the patients nor the HCPs reported any major obstacles with the use of Peek during the examination. However, the following themes emerged from all parties as potential system-related challenges in implementation that need to be considered for deployment.

Government Involvement

Lack of integration with the national health system and potential lack of government involvement were seen as major challenges to deploying Peek. Early involvement of government, policy makers, and health management teams in decision-making was therefore considered by stakeholders and HCPs to be essential to ensure sustainability of the program. These participants proposed working with the government at all stages from development to implementation. State involvement was also regarded as essential to gain public trust in the intervention; integrate services; and setting guidelines, standards, and protocols for national implementation and adoption.

Funding

Lack of funding was discussed as a barrier to deployment and sustainability of the program. Government support and partnership with NGOs was put forward as a solution to increase availability and affordability of Peek and integration with existing services. The new health restructuring in Kenya, where management has been devolved to county level, was perceived to be most likely beneficial in sustaining the intervention as resources are more likely to be spent where most needed. However, the priority given to eye health nationally was seen by the stakeholders to influence any future decisions about funding. Moreover, as indicated by one stakeholder, a cost-benefit analysis and evidence for effectiveness are essential for obtaining funding.

Other options suggested for funding were donor support for financing and other resources required for the program. Stakeholders also suggested that the government would financially benefit from adopting Peek, as it is perceived to be cost-effective compared with traditional ophthalmic testing methods.

> *From an economist point of view, I would say it is a good, it is a project worth financing*. [Stakeholder #3]

Communication and Technology Awareness

Although none of the patients expressed any reservations or fear of being examined by Peek, some mentioned that there is a possibility that certain people may not understand the purpose and value of the application. Another perceived barrier to adoption of using Peek was miscommunication. For instance, initially 1 patient reported having reservations about the use of Peek but was comfortable with it as soon as the examination steps were clearly explained. Furthermore, acceptance was also deemed to be governed by the level of education. Therefore, the importance of familiarity with MPs and the need for good communication on the utility of Peek were highlighted by several patients, HCPs, and stakeholders. Some examples were given for reasons of possible misunderstanding in the community, such as the phone being used to take patient's pictures instead of retinal images, cultural reservations about MPs, and fear of MPs having negative health effects.

> *Counselling and sharing with them and giving them reason as to why, especially if the patient needs examination, you just understand the patient and help the patient to understand*. [HCP #6, female]

Training and Product Support

A potential challenge mentioned by both stakeholders and HCPs is the need for setting up training for using Peek and product support if it were to be deployed sustainably. Consequently, they suggested the need to plan for a strong support team. Nevertheless, Peek was perceived as more sustainable than traditional equipment, with less likelihood of requiring replacement of expensive components. From patients' point of view, equipment quality was an important factor to ensure a high standard of care provision.

> *...it is more sustainable than the equipment we are providing and that is what I see. Because if these equipment breakdown, they have to be serviced and they have to buy spare parts, of which right now we have several equipment that are not working because of spare parts*. [Stakeholder #4]

Data Protection

According to HCPs and stakeholders, maintaining confidentiality of patient information is paramount and a potential barrier to sustainability and acceptability of the intervention. They proposed the need to ensure that a robust and secure data encryption system is in place. In addition, good communication was also reported as necessary to ensure that patients understand and are reassured about confidentiality. One stakeholder involved in building a central ophthalmic data collection unit, the Ophthalmic Service Unit designed to be linked to Hospital Management Information Systems, stated that it has been difficult to implement the system in Kenya. The suggestion for the implementation process was that it is important to link patient data, collected using Peek, to the HCPs' clinic as well as the central database for safekeeping.

Another issue raised was that mobile phone devices could be stolen when used in insecure remote areas, therefore reinforcing the need for robust security measures in addition to a data protection system.

Community Involvement

Stakeholders and HCPs described the benefits of training the local population for community mobilization. They suggested that training the local population to run the program will overcome any potential obstacles related to acceptability and sustainability. Patients saw the importance of community participation as key to building trust and confidence in the program and put the population at ease. From one stakeholder's point of view, getting public support is also very important to tackle cultural barriers. One patient referred to the M-Pesa service as an example of a program that has managed to drive community mobilization.

> *...early involvement and train locally available people to actually address some of those bugs that can arise that can cause a problem...* [HCP #3, male]

Increase in Demand for Ophthalmic Treatments

One obstacle mentioned was that the HS may not be able to cope with managing the increase in cases detected by Peek. A solution suggested by both HCPs and stakeholders to combat this problem is recruiting CHVs. The value of Peek in supporting HCPs who have limited training in eye care playing the role of CHVs has been highlighted throughout this study. Moreover, a stakeholder mentioned how Peek can be used to prioritize cases, which helps with shifting demand and coping with increasing workload. One stakeholder also proposed to introduce Peek to those trainees in the community who will become future HCPs.

Infrastructure

The accessibility of MPs and infrastructure supporting the use of mobiles was reported as being key for sustainability of Peek by HCPs and stakeholders. Infrastructure-related barriers raised were shortage of devices and poor mobile network provision and internet coverage, making it difficult to send across images and patient information to the central database as well as other HCPs for advice. They proposed partnering with and acquiring support from key network providers to increase availability and affordability of both the device and mobile data usage. Power shortages in rural areas leading to inability to charge phones were also mentioned as potential barriers to service delivery with Peek. Provision of HCPs with a battery-powered charging system and backing up data were given as potential solutions.

> *You know the challenges of network in Kenya, the downs, you know sometimes it just disappears in some areas and especially in the villages, in the remote areas*. [Stakeholder #2]

Discussion

This qualitative study offers a comprehensive understanding of the potential value and barriers to the deployment of the smartphone-based eye examination system, Peek, in developing countries with limited coverage of ophthalmic services. Peek as a stand-alone system is useful; however, in conjunction with smartphone functionalities it offers a highly desirable advantage. To date, studies evaluating mHealth have mainly assessed basic use of MP technology with limited evidence on the value of using smartphones for health care [7,12]. This study showed that Peek is an acceptable examination kit for HCPs, patients, and stakeholders and has the potential to strengthen the delivery of eye care in resource-poor contexts. The study has also illustrated the potential challenges and facilitators that are likely to affect the adoption and deployment of Peek.

The analysis of the user, task, technology, and environment gives an overall understanding of the context in which Peek is being evaluated. The patient diversity, patient demographics, and the HCP roles and experience utilized in this study are considered to be the representative environment for which Peek has been designed and in which it will likely be deployed. Most HCPs had limited ophthalmic specialist training, serving as CHVs with experience restricted to the year in which the Peek study was undertaken. This has provided useful insights, because if Peek were to be deployed, it is likely that CHVs will be recruited because of the shortage of ophthalmic professionals in developing countries.

Overall, HCPs demonstrated a good understanding of the utility of Peek, that is, its task. The analysis of attitudes toward technology revealed that HCPs, patients, and stakeholders perceived the population as being familiar with MPs and receptive to them being used. These views reflect the increasing penetration of MPs and more specifically smartphones in Kenya. This enthusiasm for MPs has been greatly influenced by a number of initiatives: M-Pesa's money transfer initiative that has driven MP usage in the remotest of settings and Safaricom's initiative to make smartphones more affordable through the introduction of cheaper android devices, which have led to increasing smartphone subscriptions [11].

The analysis of the context also revealed significant barriers to seeking and accessing ophthalmic services in the current HS. Both HCPs and patients felt that there was a rural–urban disparity with almost no established services in rural settings. This was reported to lead to patients having to travel long distances, having to encounter long waiting times at overburdened government facilities, and having a lack of awareness about timely detection and treatment.

Peek was found to be acceptable to patients, all of whom expressed being satisfied with Peek. Moreover, the analysis revealed that contentment with the service was often related to the quality of service provision. Most participants supported the use of Peek because it was perceived to be fast and convenient and to be able to reach a larger population in need, in addition to overcoming the aforementioned barriers. Peek is also deemed to have generated a lot of interest among the communities and is therefore an opportunity for increasing awareness of eye health within the population. Although limited, a handful of studies have shown the value of mHealth initiatives in creating awareness, for instance, in general health, HIV/AIDS, and women's health in low-income countries [34].

The analysis of the usability of Peek based on predefined usability dimensions demonstrated that per HCPs' perceptions, Peek generally fulfills the criteria for all dimensions assessed. These included efficiency, effectiveness, learnability, and operability and flexibility. In addition to the usability of Peek, the analysis confirms that Peek is acceptable to HCPs. This was demonstrated by their perceived ability to use Peek easily, fulfill their role, and meet the challenges of ophthalmic provision.

An analysis of the views of HCPs and stakeholders using a model adapted from relevant literature showed the value of Peek in strengthening the HS's ability to provide eye services [30-33]. Peek was perceived to be a capabilities enhancer for HCPs through the provision of diagnostic and decision support. This has already been introduced as an important feature of mHealth initiatives in supporting HSs as proposed in current literature [9,33]. The possibility of using Peek as a screening tool is also discussed under this theme, and its success is thought to be dependent on being able to prove its accuracy, sensitivity, accessibility, and ability to offer a high standard of service delivery. It is therefore vital that these qualities are satisfied in addition to other criteria required for enrolling a screening service before Peek can be rolled out for this purpose [38]. A

qualitative study of the accuracy of the tool has been carried out alongside this qualitative study, which has proven its accuracy, repeatability, and consistency as a vision-testing tool. Another study is also underway to determine its suitability as a screening tool in children at school.

Peek's value in creating opportunities that help in supporting health care delivery was also highlighted. These included offering eye care closer to patients and enabling monitoring and surveillance. Additionally, Peek was deemed to be a social enabler and improved communication between providers themselves as well as with their patients. Another theme highlighted was knowledge creation and development of skills by offering training opportunities. The outlined benefits of Peek show its potential value in supporting CHVs in providing a high standard of care through its inbuilt functions, because these support decision making as well as communicating with qualified ophthalmic professionals who can offer advice remotely. Other studies of mHealth in developing countries have demonstrated the value of MPs in tackling the current barriers to service provision and improving the range and quality of services offered by CHVs [34,39,40]. Moreover, these benefits are likely to play an important role in the near future, with the increasing double burden of disease in Africa where chronic ophthalmic conditions, such as glaucoma, age-related macular degeneration, and diabetic retinopathy, are also likely to become more prevalent. As a consequence, the need for Peek to be offered within a well-coordinated HS that is capable of screening for and managing these conditions as part of secondary prevention efforts is likely to become increasingly essential.

Given the paucity of studies and established guidelines on large-scale implementation of mHealth, the views of all parties gathered during this qualitative analysis assisted in understanding the challenges and facilitators in deploying Peek.

This analysis brought out several common themes that highlight key considerations that are likely to affect adoption of Peek. Many of the challenges reported are similar to those mentioned in previous mHealth studies [41]; however, several unique considerations were also revealed that are specific to Peek and the context in which it is likely to be implemented. The themes that emerged included the need for (1) government support and involvement in deployment, (2) building capacity to train HCPs and maintenance of Peek, (3) maintaining a high standard of care and good communication about the purpose of using Peek with all patients, (4) community mobilization, (5) increasing capacity to manage increasing demand for eye treatments, (6) ensuring general eye health awareness and linking with primary health care, (7) ensuring data protection, (8) ensuring accessibility to smartphone technology at low cost, and (9) infrastructural support such as mobile charging systems and improved network coverage. These considerations serve as guidance for the future implementation of Peek.

Although previous mHealth studies have been conducted on a small scale, a review of literature has shown that there is a clear opportunity for successful mHealth interventions when proven to be acceptable, accessible, easy to use, affordable, appropriate to the local context, and integrated within the HS [8,39,42-46]. Peek therefore shows promise for success.

Limitations

Since the qualitative analysis was carried out on data that had been collected retrospectively, there was limited opportunity for an iterative process whereby initial data analysis can guide further interviews. Moreover, in an attempt to answer specific predefined objectives, data were collected from semistructured interviews, which limited open-ended questions. Additional open-ended questions would have allowed for a more in-depth exploration of themes.

Conclusion

The analysis of context illustrated the perceived importance of addressing rural-urban disparity and thereby the need to increase access and coverage of ophthalmic provision. The key barriers highlighted were cost, distance, time, and lack of awareness of the importance of timely detection and treatment. From the analysis of patient, stakeholder, and user views regarding Peek, it can be concluded that Peek offers an acceptable solution to overcoming barriers to access to eye care, fulfills the criteria for usability for HCPs, and acts as a means to strengthen eye care delivery. Peek is perceived to be valuable predominantly in increasing coverage in rural settings, thereby contributing to the third global goal for sustainable development [47]. As proposed by the HCPs and stakeholders, it is also likely to have a bearing on reducing burden on ophthalmologists who with the help of CHVs using Peek can now work remotely through task shifting. To successfully deploy Peek and achieve universal coverage, it is considered imperative to build a sustainable model by integrating and working with the government, local communities, and NGOs. Ongoing research would be required to evaluate the processes of deployment and to assess whether the benefits outlined translate to improved eye health outcomes and public health indicators.

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Conflicts of Interest

None declared.

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Abbreviations

CHV: community health volunteer
HCP: health care provider
HS: health system
mHealth: mobile health
MP: mobile phone
NGO: nongovernmental organization
Peek: Portable Eye Examination Kit
SMS: short message service
TAM: Technology Acceptance Model
VA: visual acuity
WHO: World Health Organization

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Photo essay

Photo essay

Increasing access to eye care . . . there's an app for that. Peek: smartphone technology for eye health

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Peek, the Portable Eye Examination Kit, was developed and validated alongside a cohort study of eye disease in Nakuru, Kenya.[1] In the cohort, the majority of participants with visual impairment were elderly, difficult to reach and had little or no access to eye care. Expertise and ophthalmic equipment required to perform a comprehensive eye examination in areas with poor or no road access, no electricity and considerable distances from the main towns and cities leads to an inverse relationship between eye care provision and eye care needs.[2]

In the past decade, mobile phone penetration has grown to reach near ubiquity in many of the most remote parts of

Figure 1. A long queue of patients awaiting assessment in a rural village in Kenya in the Nakuru Eye Disease Cohort Study and validation of Peek

Figure 2. A secondary school used as a temporary clinic in the Nakuru Eye Disease Cohort Study and validation of Peek; note the use of blackout blinds and a generator for the ophthalmic equipment

Figure 3. A solar-powered rucksack as used by the Peek healthcare workers visiting patients door to door, negating the need for a mains power supply

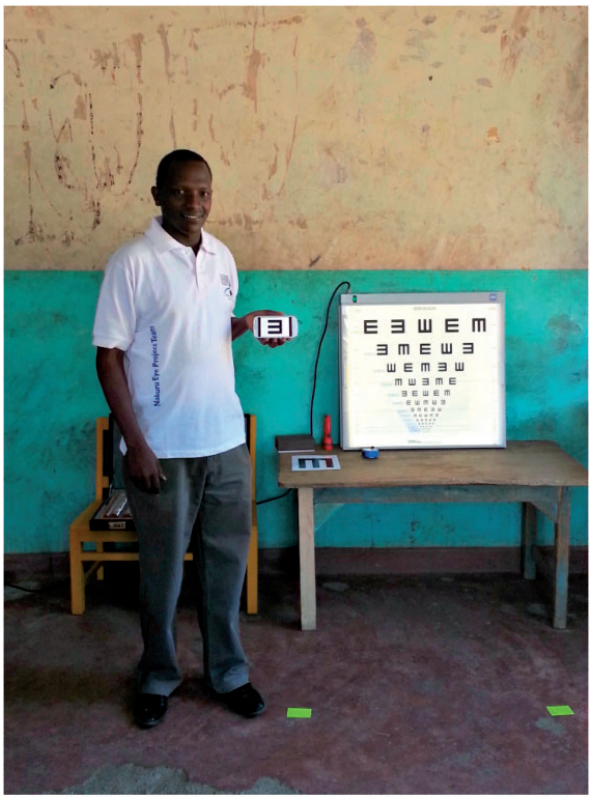

Figure 4. Validation of the Peek Acuity app measured against the reference standard LogMAR vision chart

Figure 5. Peek Acuity being measured in a patient's home in rural Kenya

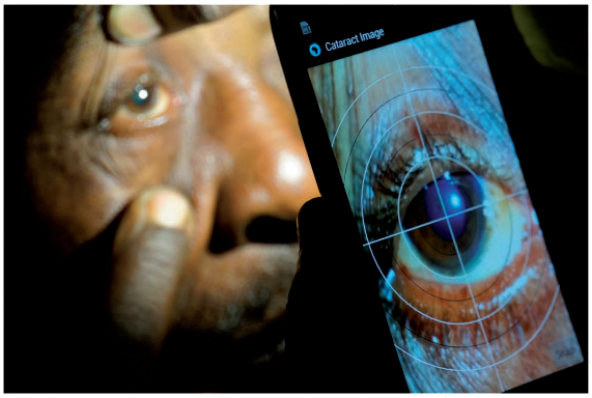

Figure 7. Examination of the lens for cataract using Peek in rural Kenya

Figure 6. Peek Acuity being tested in the hands of a non-healthcare worker in the Massai Mara

Figure 8. A Peek fieldworker examining a patient's retina in their home in rural Kenya

the world. The growth has been greatest in low- and middle-income countries (LMIC) with some countries having, on average, more than one connected device per person of population.[3]

Despite areas of Kenya and other LMIC having no access to clean running water and sanitation services, the majority do have mobile phone connectivity. Peek harnesses the portability and connectivity of mobile devices to enable task-shifting and the ability to undertake a comprehensive eye examination at, or close to, the patient's home.

The primary measure on which ophthalmic assessments are made is distance visual acuity. This is typically done using a Snellen chart or, for research purposes, a

Figure 9. A Peek fieldworker examining a patient's retina in the validation clinic in Kenya

LogMAR chart which overcomes many of the limitations of the commonly used Snellen chart. The LogMAR chart requires a power source, is not designed to travel and is not practical for use outside a clinical setting. Peek Acuity is an accurate, repeatable and fast method to test acuity using a smartphone.[4] The test uses the touchscreen interface to record participant's responses without the user needing to see the screen. This makes the test both faster and more objective. The inbuilt luxmeter, usually used to control screen brightness, can give the user a warning when ambient light levels are too bright to provide a reliable reading.

Peek Retina, a low-cost smartphone adapter, makes it possible to examine the retina using a smartphone.[5] The user only needs to be able to acquire images, and expert graders can review images remotely and action decisions without having to be away from busy eye units.

With the majority of the world's blind and visually impaired people living in LMIC, and 80% of these having a condition that is reversible or preventable,[6] it is vital that we reduce the barriers to accessing basic eye care.

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Conflict of interest: Dr Andrew Bastawrous is Founder & CEO of the Peek Vision Foundation, a UK registered charity.

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Appendix IV – Published papers from the baseline study

1. The Nakuru Posterior Segment Eye Disease Study Methods and Prevalence of Blindness and Visual Impairment in Nakuru, Kenya [7p]

2. Prevalence and Correlates of Diabetic Retinopathy in a Population-based Survey of Older People in Nakuru, Kenya [9p]

3. Prevalence of Age-Related Macular Degeneration in Nakuru, Kenya: A Cross-Sectional Population-Based Study [11p]

4. Prevalence and predictors of refractive error and spectacle coverage in Nakuru, Kenya: a cross-sectional, population-based study [8p]

The Nakuru Posterior Segment Eye Disease Study

Methods and Prevalence of Blindness and Visual Impairment in Nakuru, Kenya

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Objectives: To estimate the prevalence of blindness and visual impairment (VI) in adults aged ≥50 years in the Nakuru district of Kenya and to identify sociodemographic risk factors for these conditions. We also sought to validate the Rapid Assessment of Avoidable Blindness (RAAB) methodology.

Participants: There were 5010 subjects enumerated for this study. Of these, 4414 participants underwent examination, for a response rate of 88.1%.

Design: Cross-sectional, population-based survey.

Methods: Cluster random samplings with probability proportionate to size procedures were used to select a representative cross-sectional sample of adults aged ≥50 years. Each participant was interviewed, had distance visual acuity (VA) measured with reduced logarithm of the minimal angle of resolution tumbling-E chart, underwent autorefraction, and thereby had measurements of presenting, uncorrected, and best-corrected VA. All participants, regardless of vision, underwent detailed ophthalmic examinations including slit-lamp assessment and dilated retinal photographs.

Main Outcome Measures: Visual acuity of <6/12.

Results: A representative sample of 4414 adults were enumerated (response rate, 88.1%). The prevalence of blindness (VA < 3/60 in better eye) was 1.6% (95% confidence interval [CI], 1.2–2.1%) and of VI, 0.4% (95% CI, 0.3–0.7%); 8.1% (95% CI, 7.2–9.2%); and 5.1% (95% CI, 4.3–6.1%) were severely (<6/60–3/60), moderately (<6/18–6/60), or mildly (<6/12–6/18) visually impaired, respectively. Being male, having less education, having Kalenjin tribal origin, and being ≥80 years old were associated with increased blindness prevalence. Prevalence estimates were comparable to a RAAB performed in the same area 2 years earlier.

Conclusions: This survey provides reliable estimates of blindness and VI prevalence in Nakuru. Older age and tribal origin were identified as predictors of these conditions. This survey validates the use of RAAB as a method of estimating blindness and VI prevalence.

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The World Health Organization (WHO) estimates 285 million people are visually impaired worldwide, 39 million are blind (<3/60), and 246 million have visual impairment (VI; <6/18–3/60).[1] The highest prevalences of blindness and VI are in Africa, with 7 million blind and 27 million with VI, although a lack of data on prevalence and causes of low vision in Africa was highlighted in the report.[2] The population of Africa is not homogenous, and so country-specific data are required if the goals of "VISION 2020: The Right to Sight" global initiative to eliminate avoidable blindness by 2020 are to be met. Avoidable blindness is defined as blindness that could be either treated or prevented by known, cost-effective interventions. Consequently, VISION 2020 seeks to address the main causes of avoidable blindness, cataract, refractive error, trachoma, onchocerciasis, and childhood blindness to have the greatest possible impact on vision loss worldwide.

The majority of survey data from Africa are based on nonstandardized methodology with a preponderance for areas with endemic diseases such as trachoma or onchocerciasis. Since completion of the WHO systematic review in 2002,[2] a new methodology has been proposed, the Rapid Assessment of Avoidable Blindness (RAAB),[3] which is a rapid, standardized survey and examination methodology to assess the prevalence of blindness and VI and avoidable causes of vision loss. To date, in Africa, there have been RAABs published from Kenya,[4] Rwanda,[5] Eritrea,[6] Malawi,[7] Tanzania,[8] and Zanzibar.[9]

Large, national, population-based surveys, such as those undertaken in The Gambia,[10] Ethiopia,[11] and Nigeria[12] are expensive and time consuming; accurate diagnosis of all causes of blindness and VI require expensive and cumbersome equipment that is infrequently used in field-based surveys. Therefore, the RAAB provides a rapid, low-cost alternative.

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Nakuru district (now Nakuru county) is the main district of Kenya's largest province, the Rift Valley province, and has a population of 1.6 million. Nakuru district is broadly representative of Kenya in terms of ethnic diversity and economic activities. The Nakuru Eye Unit based at the Rift Valley Provincial Hospital provides most of the ophthalmic services for Nakuru district, serving approximately 10 000 patients each year. A RAAB was undertaken in Nakuru in 2005 and identified that posterior segment eye disease was the second leading cause of blindness.[4] Consequently, the Nakuru posterior segment eye disease survey was undertaken to explore the prevalence and predictors of these conditions, which were not assessed in detail in the RAAB.

This study estimates the prevalence of blindness and VI in an African population aged ≥50 years in the Nakuru district of Kenya. We can also compare the results of this survey with the previously undertaken RAAB.[4] Predictors of blindness/VI in this population were also identified. The prevalence and causes of posterior segment eye disease blindness and VI will be published in a later article.

Methods/Design

The study fieldwork was carried out in 2 phases from January 2007 to June 2007 and from April 2008 to November 2008.

Sample Size Calculation

The sample size required was calculated based on an expected prevalence of a visual acuity (VA) of <6/12 in the better eye caused by posterior segment disease of 3.0% among those aged ≥50 years, a required precision of 0.5% (a 95% confidence interval [CI]), a design effect of 1.5, and a response rate of 90%, so that 4996 participants were needed (Epi Info 6.04, US Centers for Disease Control and Prevention, Atlanta, GA). We therefore aimed to select 100 clusters, each of 50 participants.

Sampling Strategy and Recruitment

Recent census data for Kenya were not available[13]; therefore, election role lists that were renewed in 2006 in preparation for the 2007 general elections were used as the sampling frame for this survey. The population size was updated for 2007 using a population growth rate of 2.7% per year.[14] We selected 100 clusters with a probability proportional to the size of the population. A cluster was defined as the area served by the polling station.

Households were selected within clusters using a modified compact segment sampling method.[15] Each cluster was divided into segments; each segment included approximately 50 people aged ≥50 years. For instance, if a cluster included 200 people aged ≥50 years, then it was divided into 4 segments. One of the segments was chosen at random by drawing lots and all households in the segment were sequentially sampled, until 50 people aged ≥50 years were identified. An eligible individual was defined as someone aged ≥50 years living in the household for ≥3 months in the previous year. Age was determined using the subject's testimony, national identity cards, and a calendar of historic events. If the segment did not include 50 people aged ≥50 years, then another segment was chosen at random and sampling continued. If after enumerating individual number 49 the next household had >1 person aged ≥50, all were enumerated and invited for examination.

Ophthalmic and General Examination

Suitable predetermined examination sites were selected on the recommendation of the village leader with close proximity for access to the cluster and electricity supply (mains or generator) for the equipment.

The examination team was led by an ophthalmologist (W.M.) who examined every participant in the study and included 2 nurses delivering questionnaires; 2 fully trained ophthalmic nurses undertook visual acuity checking and autorefraction. A trained visual field technician performed field tests, an ophthalmic clinical officer took fundus photographs, and another nurse took weight, height, blood pressure, and blood tests. The team also included an office manager and 2 data entry clerks.

Visual Acuity

The presenting another VA was defined as the number of letters read correctly without glasses if the participant did not have glasses or with glasses if they had them. Testing was done by an ophthalmic nurse with an assistant. Each eye was tested separately at 4 m using a reduced logarithm of the minimal angle of resolution tumbling "E" chart[16] in a well-illuminated area. If the subject's vision was too poor to read any letters on the chart at 4 m, then the subject was tested at 1 m, then as follows:

- Counting fingers: Ability to count fingers at 1, 2, or 3 m distance;
- Hand motion: Ability to distinguish whether a hand is moving in front of the patient's face;
- Light perception: Ability to perceive any light; and
- No light perception: Inability to see any light or total blindness.

Those who did not read 24 letters (VA <6/12) at 4 m were scheduled for correction and to undergo a repeat VA measurement with the correction in place, unless the vision was worse than counting fingers, in which case no correction was undertaken (Table 1).

Diagnosis of Causes of Blindness

Cataract. Participant's pupils were pharmacologically dilated to a minimum of 6.5 mm (tropicamide 1%). Anterior segment examination was performed at the slit lamp by the ophthalmologist. The lens was graded using the WHO simplified system.[17]

Refractive Error. An automated Topcon autorefractor RM8800 (Topcon, Oakland, NJ) was used to provide an objective measurement of all participants' refractive error and their prescription for glasses regardless of VA. For purposes of this study, the printout contained readings of the sphere (–25 diopters [D] to +22 D [to

Table 1. Visual Acuity Categories Used in the Study

Visual Category	Reduced LogMAR Letters Seen	Snellen Equivalent	LogMAR Score Equivalent
Normal	≥24	6/12	0.0–0.3
Mild VI	19–23	<6/12–6/18	<0.3–0.48
Moderate VI	3–18	<6/18–6/60	<0.48–1.0
Severe VI	2	<6/60–3/60	<1.0
Blindness	0.1	<3/60	

LogMAR = logarithm of the minimal angle of resolution; VI = visual impairment.

the nearest 0.25 D]), cylinder (0 to ±10 D [to the nearest 0.25 D]), and axis (0°–180° [in 5°steps]). Uncorrected, presenting, and autorefractor-corrected (using trial frames and lenses) VA were measured on all participants.

Visual Field Testing. The Humphrey Field Analyzer II 720*i* series (Carl Zeiss Ophthalmic Systems, Inc., Peabody, MA) was used for automated visual field testing in eligible individuals as well as in a random sample of 5 individuals per cluster identified during enumeration.

Participants performed the Swedish Interactive Thresholding Algorithm Standard 24-2. Every participant underwent the Swedish Interactive Thresholding Algorithm Fast (quick test) to determine their threshold level. Appropriate corrective lenses for refractive errors were used when needed; if the results were unreliable (false-positives, >20%; false-negatives, >33%; fixation losses, >33%), the participant then repeated the test once more.

Fundoscopy and Lens Grading. Pharmacologic dilation of the participant's pupils was performed using 1 drop of tropicamide 1%. Examination of the anterior chamber as well as the lens was performed at the slit lamp by the ophthalmologist (W.M.) to identify causes of reduced visual acuity or reasons for reduced clarity of the posterior segment.

The optic nerve was examined using a 90-D lens at the slit lamp; the clarity of the view of the optic nerve head was determined and graded as clear, hazy, or no view depending on whether there was a complete view of the retinal details, incomplete view, or nothing visible, respectively. Among subjects in whom an adequate view of the disc was available, the vertical cup-to-disc ratio was estimated and recorded. Any asymmetry ≥0.2 between the 2 eyes was noted. Other characteristics of the optic nerve including notching of the rim, vessel location perturbations, nerve fiber layer defects, nonglaucomatous optic atrophy, and optic nerve head hemorrhages were also recorded. If only 1 eye could be visualized, then asymmetry was recorded as "not applicable."

Retinal Examination. Slit-lamp biomicroscopy with a 90-D lens involved an assessment of the macula, the retinal vasculature, and the peripheral retina. The view of the retina was recorded as clear, hazy, or no view, and the optic disc was assessed as outlined above. Diabetic retinopathy was graded and recorded as absent, nonproliferative, maculopathy (macula edema), proliferative, or end stage (UK National Guidelines on Screening for Diabetic Retinopathy, NHS 2010). The macula was examined for presence of drusen, hypopigmentation, or hyperpigmentation, dry or geographic atrophy, and neovascular changes. Any other pathology of the retina or vitreous, for example retinal detachments or vitreous hemorrhages, were also noted and a description given.

Fundus Photography. The participants had 2 nonstereoscopic, digital, 45° fundus photographs taken per eye by an ophthalmic clinical officer using a TRC-NW6S Non-Mydriatic Retinal Camera with 10 megapixel Nikon D80 (Topcon). The images were digitally stored using the preinstalled IMAGEnet Telemedicine System. One image was centered on the optic disc while the other was centered on the macula. Images were forwarded to the Retinal Grading Centre at Moorfields Eye Hospital Reading Centre in London for grading and confirming the clinical diagnosis of posterior segment disease. The digital photographs were graded by a dedicated certified grader. Moorfields Eye Hospital Reading Centre is a certified Wisconsin Reading Center. All images were first categorized for quality as excellent, good, fair borderline, or ungradeable. Images were graded separately for age-related macular degeneration, diabetic retinopathy, and optic disc pathology.

Other. The presence or absence of trachoma, corneal scarring, globe abnormalities, and any other pathology was recorded.

General Information. Detailed interviews were undertaken in the local language covering demographic details, information on risk factors, socioeconomic status, and full medical history. We also measured weight, height, waist and hip circumference, blood pressure, and random cholesterol and glucose blood levels.[18] "Mother tongue" was used as a measure of tribal affiliation.

Visual Impairment and Blindness Definitions. Based on the VA test used in this study, VI was defined by the number of letters read (Table 1).

Data Entry

A data entry package in EpiData Entry v 2.1 was developed for this study, which incorporated range and consistency checks. If an error was detected, the data entry clerks asked the field team at the end of the same day, and the error could thus be rectified or missing information collected on the next day. Data from each questionnaire were entered by 2 different people, on 2 separate computers. Consistency checks were performed each evening and inconsistencies corrected the same day. Two datasets, one for the demographic and risk factor information and one for the ophthalmic examinations, were stored, each bearing the same study identification number.

Data Analysis

Prevalence of blindness and VI was estimated, and the cluster design of the study was taken into account by using the "svy" commands in STATA (Stata Corp, Inc., College Station, TX) when calculating CIs around the prevalence estimates.

Socioeconomic Status. A continuous asset score was produced for each participant using principle component analysis. The score was divided into quartiles to categorize the study participants into 4 socioeconomic groups, with a higher score representing higher socioeconomic status.

Obesity. Using body mass index (height [m]/weight [kg^2]) was categorized as <18.5 (underweight), 18.5 to 24.99 (normal), 25 to 29.99 (overweight), ≥30 (obese), 30 to 34.99 (obese class 1), 35 to 39.99 (obese class 2), or ≥40 (obese class 3). Obesity using waist circumference was categorized using WHO guidelines[19] as normal (male, <94 cm; female, <80 cm), overweight (male, 94–101.9 cm; female, 80–87.9 cm), or obese (male, ≥102 cm; female, ≥88 cm).

The clusters were defined as rural or urban according to the classification used by the District Health Statistics office.[20] The distinctions were made nationally based on population density, administrative function, and availability of social amenities and physical infrastructure such as hospitals, post office, schools, and markets.

Potential risk factors for blindness were identified after assessment of the literature. Logistic regression analyses were produced to assess the univariate associations between potential risk factors and prevalent blindness. Inclusion in the multivariable logistic regression was by purely statistical criteria, retaining those variables that were significant correlates of blindness, always retaining age and gender in the model.

Ethical Approval

Ethical approval was granted by the London School of Hygiene and Tropical Medicine ethics committee and also the Kenya Medical Research Institute. Approval was also granted by the Provincial Medical Officer Rift Valley and the Nakuru district Medical Officer of Health. Written approval was sought from the administrative heads in each cluster, usually the village chief. All participants gave written or verbal consent to participate. Those requiring medical treatment were referred to the appropriate center.

Table 2. Age and Gender Composition of District and Sample Populations

Age Groups (yrs)	Male		Female		Total	
	District (n = 44 519)	*Sample (n = 2113)*	*District (n = 44 195)*	*Sample (n = 2301)*	*District (n = 88 714)*	*Sample (n = 4414)*
50–54	13 907 (31%)	428 (20%)	13 721 (31%)	565 (25%)	27 628 (31%)	993 (23%)
55–59	10 081 (23%)	428 (20%)	10 076 (23%)	528 (23%)	20 157 (23%)	956 (22%)
60–64	7432 (17%)	376 (18%)	7412 (17%)	380 (17%)	14 844 (17%)	756 (17%)
65–69	5482 (12%)	271 (13%)	5452 (13%)	277 (12%)	10 934 (13%)	548 (12%)
70–74	3753 (8%)	242 (12%)	3706 (11%)	206 (9%)	7459 (8%)	448 (10%)
75–79	2208 (5%)	165 (8%)	2205 (5%)	128 (6%)	4413 (5%)	293 (7%)
≥80	1656 (4%)	203 (10%)	1623 (4%)	217 (9%)	3279 (4%)	420 (10%)

Results

Study Participation and Response Rates

There were 5010 subjects enumerated for this study. Of these, 4414 participants underwent examination, for a response rate of 88.1%. The response rate was similarly high among men (89.2%) and women (86.5%). Of the nonrespondents, 584 (98%) were away working or visiting family outside the cluster location and 12 (2%) refused to participate; none were excluded as a result of inability to communicate.

Comparison of Responders and Nonresponders

Details about gender were available for all of the nonresponders, whereas age was available for 526 nonresponders (90.1%). Those who were examined were significantly older (mean age, 63.4 years; standard deviation, 10.5 years) than those who were not (mean, 61.9 years; standard deviation, 10.6 years; $P = 0.002$). Women were significantly overrepresented among the nonresponders (56.8%) compared with those who were examined (52.1%; $P = 0.03$). Among those enumerated, 66.5% were from rural clusters; among those who were examined, 67.2% were rural ($P = 0.7$). Of those who were not examined, none were believed to be blind.

Among those who responded, 33 had incomplete examinations or missing data. Fifteen of these had complete demographic information including blood tests. Therefore, 4396 participants are included in the baseline characteristics descriptions and 4381 in the ophthalmic analyses.

Comparison of District and Sample Populations

The sample population was slightly older than the general population (P for chi-square < 0.001) and women were relatively overrepresented (P for chi-square $= 0.003$; Table 2). However, the district estimates for age and gender distribution were based on census data 10 years old and so may not have been reliable.

Population Descriptions

The majority (63%) of participants were Kikuyu, the largest ethnic group in Kenya. Kalenjin formed 23% of the sample population, and 5 other tribes constituted 7.5% of the total. One third of participants (33%) had no education and almost 10% had tertiary education. Of the participants, 67.3% were from rural clusters.

Blindness and Low Vision for Nakuru and for Kenya

Of the sample, 1.6% (95% CI, 1.2%–2.1%) were bilaterally blind, 0.4% (95% CI, 0.3%–0.7%), 8.1% (95% CI, 7.2%–9.2%), and 5.1% (95% CI, 4.3%–6.1%) were severely, moderately, or mildly visually impaired, respectively, based on presenting VA (Table 3). Overall prevalence of blindness was greater among men than women.

The estimates were extrapolated to estimate the magnitude of blindness and VI in adults aged ≥50 years in Nakuru (Table 4). Based on the study findings, it is estimated that 1419 adults ≥50 years are blind in Nakuru district.

Visual Acuity by Age

Advancing age was associated with greater prevalence of VI. In the age group 50 to 59 years, 95.5% had normal vision (VA ≥ 6/12 in both eyes); however, only 42.7% in the ≥80 age group had normal vision. Of adults ≥80 years, 9.1% were blind compared with 0.5% in the 50 to 59, 0.9% in the 60 to 69, and 1.5% in the 70 to 79 years age groups (Fig 1).

After correcting for refractive error the prevalence of blindness with best-corrected VA was 1.1% (95% CI, 0.8–1.5). The preva-

Table 3. Prevalence of Blindness and Visual Impairment (VI)

Presenting Visual Acuity in the Better Eye (Snellen) (LogMAR Letters)	Male (n = 2099)		Female (n = 2282)		Total (n = 4381)	
	n	*Prevalence (95% CI)*	*n*	*Prevalence (95% CI)*	*n*	*Prevalence (95% CI)*
Blind (<3/60) (0–1)	44	2.1% (1.5–2.9)	27	1.2% (0.8–1.8)	71	1.6% (1.2–2.1)
Severe VI (<6/60–≥3/60) (2)	11	0.5% (0.3–0.9)	7	0.3% (0.2–0.6)	18	0.4% (0.3–0.7)
Moderate VI (<6/18–≥6/60) (3–18)	175	8.3% (7.1–9.7)	181	7.9% (6.8–9.2)	356	8.1% (7.2–9.2)
Mild VI (<6/12–≥6/18) (19–23)	105	5.0% (4.1–6.1)	119	5.2% (4.1–6.9)	224	5.1% (4.3–6.1)
Normal vision ≥6/12 (≥24)	1764	84.0% (82.0–85.9)	1948	85.4% (83.0–87.4)	3712	84.7% (82.9–86.4)

CI = confidence interval; LogMAR = logarithm of the minimal angle of resolution.

Table 4. Magnitude of Blindness in Those >50 Years in Nakuru District, Kenya

Age (yrs)	Population Size in Nakuru, n (%)	Blindness		SVI		Moderate VI	
		Prevalence (%)	*Expected No. of Cases (95% CI)*	*Prevalence (%)*	*Expected No. of Cases (95% CI)*	*Prevalence (%)*	*Expected No. of Cases (95% CI)*
50–59	47 785 (54)	0.5	239 (143–478)	0.1	48 (10–191)	1.9	908 (669–1195)
60–69	25 778 (30)	0.9	232 (129–412)	0.4	103 (52–232)	6.1	1573 (1186–2088)
70–79	11 872 (13)	1.5	178 (95–332)	0.1	12 (5–119)	15.0	1781 (1460–4286)
80+	3279 (4)	9.1	298 (203–433)	2.4	79 (43–141)	31.3	1026 (879–1184)
Total	88714	1.6	1419 (1065–1863)	0.4	355 (266–621)	8.1	7186 (6387–8162)

CI = confidence interval; SVI = severe visual impairment; VI = visual impairment.

lence of mild, moderate, and severe VI with best correction was 2.3% (95% CI, 1.8–3.1), 3.5% (95% CI, 2.9–4.2), and 0.2% (95% CI, 0.1–0.4), respectively. The prevalence of best-corrected VA blindness was higher in men than women (1.4% vs 0.8%) but did not attain significance.

Age and Gender. Age- and gender-adjusted logistic regression analyses (Table 5) revealed that the prevalence of blindness increased significantly with age in the ≥80 years age group, carrying 18.8 times (95% CI, 9.2–38.1) higher odds of blindness than those aged 50 to 59 years. Females had 40% lower odds of blindness than men (0.6; 95% CI, 0.4–0.9). Compared with people with no education, the odds of blindness was lower among those with 1 to 7 years of education (odds ratio [OR], 0.3; 95% CI, 0.1–0.5), or >7 years of education (OR, 0.2; 95% CI, 0.1–0.7). Odds of blindness was similar for those residing in rural compared with urban locations (OR, 1.0; 95% CI, 0.6–1.8). Participants with diabetes had more than twice the odds of blindness compared with nondiabetics (OR, 2.3; 95% CI, 1.1–4.7%); however, the association with hypertension was not significant (OR, 1.2; 95% CI, 0.8–2.0). There was no clear relationship between blindness and smoking or drinking. Those from the Kalenjin tribe had 2.5 times higher odds of blindness (95% CI, 1.5–4.1) than those of the Kikuyu tribe or others.

Using stepwise multivariate regression analysis and adjusting for all factors significant at the $P \leq 0.05$ level, male gender ($P = 0.003$), education level ($P < 0.0001$), Kalenjin tribe ($P = 0.003$) and age ≥80 years ($P < 0.0001$) were associated with increased odds of blindness. Diabetes ($P < 0.09$) and hypertension ($P < 0.08$) had borderline associations with increased odds of blindness.

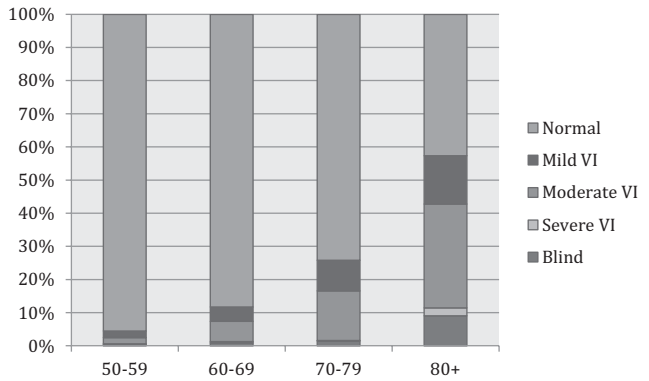

Figure 1. Distribution of visual impairment by age.

Table 5. Risk Factors for Blindness (n = 4314)

	Blind, n (%), n = 71 (1.6%)	Age-adjusted OR (95% CI)	Multivariate-Adjusted OR (95% CI)
Age (yrs)			
50–59	10 (0.5)	Baseline	Baseline
60–69	12 (0.9)	1.7 (0.7–4.0)	NS
70–79	11 (1.5)	2.7 (1.1–6.5)	NS
≥80	38 (9.1)	18.8 (9.2–38.1)	5.8 (3.4–10.1)
Gender			
Male	44 (2.1)	Baseline	Baseline
Female	27 (1.2)	0.6 (0.4–0.9)	0.4 (0.2–0.7)
Education (yrs)			
None	51 (3.5)	Baseline	Baseline
1–7	16 (0.8)	0.3 (0.1–0.5)	0.3 (0.1–0.5)
>7	4 (0.5)	0.2 (0.1–0.7)	0.2 (0.1–0.7)
SES			
1 (poorest)	32 (2.9)	Baseline	—
2	14 (1.3)	0.5 (0.3–1.0)	—
3	15 (1.4)	0.7 (0.4–1.3)	—
4 (least poor)	9 (0.8)	0.5 (0.2–1.1)	—
Habitat			
Rural	53 (1.8)	Baseline	—
Urban	18 (1.3)	1.0 (0.6–1.8)	—
Diabetes			
No	61 (1.5)	Baseline	Baseline
Yes	10 (3.5)	2.3 (1.1–4.7)	2.1 (0.9–5.0)
Hypertension			
No	27 (1.3)	Baseline	Baseline
Yes	44 (1.9)	1.2 (0.8–2.0)	1.6 (0.9–2.8)
Smoker			
Never	45 (1.5)	Baseline	—
Former	24 (2.5)	1.2 (0.7–2.2)	—
Current	2 (0.6)	0.4 (0.1–1.9)	—
Alcohol			
Never	17 (1.0)	Baseline	Baseline
Former	49 (2.6)	1.4 (0.7–2.6)	NS
Current	5 (0.7)	0.4 (0.2–1.3)	0.2 (0.1–0.6)
Tribe			
Kikuyu	34 (1.2)	Baseline	Baseline
Kalenjin	34 (3.2)	2.5 (1.5–4.1)	2.3 (1.3–3.9)
Others	5 (0.8)	1.1 (0.4–2.9)	NS
BMI			
Normal/underweight	59 (2.1)	Baseline	Baseline
Overweight/obese	8 (0.5)	0.4 (0.2–0.8)	0.4 (0.2–0.8)

BMI = body mass index; CI = confidence interval; NS = not significant; OR = odds ratio; SES = socioeconomic status; —, not included in multivariate analysis.

Discussion

This study describes the vision status of a random sample of Kenyan people aged ≥50 years living in Nakuru district using comprehensive ophthalmic examination techniques. The results confirm that prevalence of blindness is relatively low as suggested by recent RAAB surveys[4,21] and that it may be declining compared with earlier surveys.[22]

The prevalence of bilateral blindness in this study (1.6% [95% CI, 1.2–2.1]) is similar to that found in the RAAB performed in the same district in 2005 (2.0% [95% CI, 1.5–2.4%]), whereas the prevalence of VI (Snellen <6/18–6/60) is slightly higher in this survey (8.1%; 95% CI, 7.2%–9.2%) compared with that in the RAAB (5.8%, 95% CI, 4.8%–6.8%). During the RAAB, enumeration and examination occur simultaneously, as opposed to as separate endeavors in the survey. Furthermore, VA was assessed using a simple tumbling E chart in the RAAB, compared with the more detailed logarithm of the minimal angle of resolution assessment in this survey. Finally, a simplified examination protocol using a direct ophthalmoscope is used in RAAB to assess causes of blindness, whereas in the current study the examination was in more detail with more sophisticated technology. The RAAB methodology has been field tested in a variety of settings, showing it to be a low-cost method of undertaking an ophthalmic survey. However, this is the first setting in which it has been compared with a more detailed survey protocol and found to be appropriate for assessing the prevalence of blindness.

The prevalence of blindness and VI was similar to or lower than that in recent African-based RAAB surveys among people aged ≥50 years, which varied from a prevalence of 1.8% (95% CI, 1.2%–2.4%) in Rwanda[5] to 9.0% (95% CI, 8.0%–10.0%) in Eritrea.[6] It was also considerably lower than the prevalence found in the recent Nigeria survey[12] of 4.2% (95% CI, 3.8%–4.6%) among people ≥40 years, but comparable with that of all age groups from the neighboring country of Ethiopia,[11] where the prevalence was found to be 1.6%, but 14.8% among those ≥60 years.

Tribal differences were notable, with Kalenjins being 2.5 times more likely to be blind than Kikuyus and other tribes. This may be attributed to socioeconomic status differences, with only 9% of Kalenjins being in the upper quartile compared with 26% of Kikuyus, although the association persisted after adjustment for socioeconomic status. Varying levels of awareness or vulnerability to disease may also be important. An unusually high representation of men was seen among those found to be blind. This is possibly due to district data not being representative because it was based on electoral role data and extrapolated to the proportion aged ≥50 years.

The strengths of this study include (1) a single senior ophthalmologist examining each participant, (2) a large, population-based sample, (3) high-level technological diagnostic equipment, and (4) the use of internationally accepted definitions of disease.

Limitations of this study include the restriction to inclusion of participants to adults >50 years of age. It has, however, been shown that not only is most blindness and VI found in this group, but also that restricting assessment to this group provides a good reflection of the prevalence and causes of VI in the general population while using a smaller sample size, thus reducing survey time and costs.[3] However, the high cost requirement of such a study makes it difficult to repeat, particularly in a low-income setting. Although it seems that the data from this study closely reflect that of the RAAB in the same area, the 2 studies were not performed concurrently. The relatively small number of cases of blindness may have constrained the power available to detect significant associations.

Nonrespondents were found to be slightly younger than respondents, which may lead to an overestimation of the prevalence of blindness and VI in the study population.

The Nakuru district has approximately 1419 individuals who are blind and a further 7541 with VI. The district is served by the Rift Valley Provincial Hospital, which has a 48-bed dedicated eye facility staffed by 1 ophthalmologist. There are also 2 ophthalmic clinical officers who are trained as cataract surgeons. Further resources are required to close the gap between currently available resources and need.

Data from this survey suggest a lower prevalence of blindness and VI than most African populations. It is also strongly suggestive that the RAAB methodology being used throughout Africa and worldwide is a robust and reliable methodology when adhered to and fulfills the authors' recommendations on use of the RAAB methodology[3] in a population for whom there is a more complete data set. Further work is being undertaken to assess the causes of blindness within this population.

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ORIGINAL ARTICLE

Prevalence and Correlates of Diabetic Retinopathy in a Population-based Survey of Older People in Nakuru, Kenya

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ABSTRACT

Purpose: To estimate the prevalence of and factors associated with diabetic retinopathy (DR) among people aged ≥50 years in Nakuru, Kenya.

Methods: Probability-proportional-to-size sampling was used to select 100 clusters of 50 people aged ≥50 years during 2007–2008. Households within clusters were selected through compact segment sampling. Participants underwent dilated slit lamp biomicroscopy (SLB) by an ophthalmologist and digital retinal photography. Images were graded for DR at the Moorfields Eye Hospital Reading Centre, UK. Diagnosis of DR was based on retinal images where available, otherwise on SLB. Anthropometric measures, including random glucose, and lifestyle factors were measured.

Results: We examined 4414 adults (response rate 88.1%), of whom 287 had diabetes. A total of 277 of these were screened for DR by SLB, and 195 also underwent retinal photography. The prevalence of any DR diagnosed by retinal images among diabetics was 35.9% (95% confidence interval, CI, 29.7–42.6%). The most common grade of DR was mild/moderate non-proliferative DR (NPDR; 22.1%, 95% CI 16.1–29.4%), while severe NPDR and proliferative DR were less frequent (13.9%, 95% CI 10.0–18.8%). SLB significantly underdiagnosed DR compared to retinal photography, particularly for milder grades. Of 87 individuals with DR, 23 had visual impairment (visual acuity <6/12). DR was associated with younger age, male sex, duration and control of diabetes, and treatment compliance. Coverage of photocoagulation in those needing immediate laser was low (25%).

Conclusion: DR remains a threat to sight in people with diabetes in this elderly Kenyan population. Screening diabetics may enable those requiring treatment to be identified in time to preserve their sight.

Keywords: Diabetic retinopathy, epidemiology, kenya, ophthalmology, survey

INTRODUCTION

Diabetes is a major threat to global public health. Approximately 347 million people worldwide have diabetes.[1] This figure is likely to rise substantially,[2,3] with the greatest increases expected to be in Africa and the Middle East as a result of population growth, aging, and the increase in obesity and sedentary lifestyles in these regions.[4]

Diabetic retinopathy (DR) is one of the microvascular complications of diabetes and is the most severe ocular complication of diabetes. DR is the leading

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cause of blindness in adults under 75 years in high income countries,[5,6] and is responsible for at least 1% of blindness globally.[7] The predicted rise in the proportion of adults with diabetes will inevitably lead to an increase in the prevalence of DR.[8]

There is currently little evidence available on the contribution of diabetes to blindness in African countries. This is because detection of DR in Africa remains a challenge, due to lack of necessary equipment and skilled human resources.[9] Only one population-based survey was identified for sub-Saharan Africa which included assessment of DR, which was undertaken in Nigeria and showed that DR was responsible for only 0.5% of blindness and 1.0% of low vision.[10] In a summary of hospital-based studies published in Africa the prevalence of DR in diabetic populations in the African continent varied between 16 and 55% depending on clinical site, and the duration and control of diabetes in the populations investigated.[11,12] Severe forms of DR were found in about 15% of patients.[13]

DR may occur early in the course of diabetes in Africa because of inadequate control of diabetes, co-occurring hypertension,[14] and possibly because the progression of DR is more rapid in black populations.[15] As general diabetic care improves and life expectancy for people with diabetes increases in Africa, it is likely that more DR and more blindness from DR will occur.

Data are urgently needed on the prevalence of DR in order to plan treatment and preventive services. More information is also needed on factors associated with DR in Africa, as these may differ to those in other settings. We have conducted a population-based survey of ophthalmic disease among people aged 50+ years in Nakuru, Kenya, which allows these questions to be investigated. The overall prevalence of blindness (visual acuity, VA, <3/60 in the better eye) in the survey was 1.6% (95% confidence interval, CI, 1.2–2.1%), while 0.4% (95% CI 0.3–0.7%) had severe visual impairment (VI); 8.1% (95% CI 7.2–9.2%) had moderate VI, and 5.1% (95% CI 4.3–6.1%) mild VI.[16] Refractive error was responsible for 51.7 % of overall VI.[17] The aim of the current study was therefore to estimate the prevalence and risk factors of DR among people aged 50 years and older, within this population-based survey in the Nakuru district of Kenya.

MATERIALS AND METHODS

Nakuru district has a population of 1.2 million, one third of which is urban. Nakuru is broadly representative of Kenya in terms of ethnic diversity and economic activities. The study fieldwork was carried out in two phases from January 2007 to June 2007 and from April 2008 to November 2008. Full details of the methods are presented elsewhere.[16]

Sampling Strategy and Recruitment

We selected 100 clusters of 50 people aged ≥50 years through probability proportional to size sampling, using the electoral role as the sampling frame. Households were selected within clusters using a modified compact segment sampling method.[18] The enumeration team visited households, assisted by a village guide, and invited all eligible participants aged ≥50 years to the examination clinic which would be held at a convenient place in the cluster over the subsequent 2 days. Eligible participants were defined as those aged ≥50 years resident in the cluster (i.e. living there at least 6 months per year) who had slept in the house either the night before or were planning on sleeping in the house that night. If an eligible person was absent then the survey team revisited the household at least two times.

Data Collection

At the examination clinic the following examinations were undertaken:

Visual Acuity

Two ophthalmic nurses measured presenting VA, which was defined as the number of letters read correctly without glasses if the participant did not have glasses or with glasses if they had them. Each eye was tested separately at 4 m using a reduced logarithm of the minimum angle of resolution (LogMAR) tumbling 'E' chart[19] in a well-illuminated area. If a subject's vision was too poor to read any letters on the chart at 4 m, then the subject was tested at 1 m, then counting fingers, hand movements, light perception or no light perception.

Ophthalmic Examination

An ophthalmic examination was performed at the slit lamp by the study ophthalmologist (WM). Pharmacologic dilation of the participant's pupils was performed using one drop of tropicamide 1%. Slit lamp biomicroscopy (SLB) with a 90 diopter lens involved an assessment of the macula, the retinal vasculature, and the peripheral retina. The view of the retina was recorded as clear, hazy or no view. Other signs of pathology were also recorded.[16]

Fundus Photography

Participants had two non-stereoscopic digital 45° fundus photographs taken per eye by an ophthalmic clinical officer using a TRC-NW6S non-mydriatic retinal camera (Topcon, Oakland, NJ, USA) with 10 megapixel Nikon D80 (Nikon, Tokyo, Japan). Images were digitally stored using the preinstalled

IMAGEnet Telemedicine System. One image was centered on the optic disc while the other was centered on the macula.

Retinal images were forwarded to the Retinal Grading Centre at Moorfields Eye Hospital Reading Centre, London, UK, for grading DR. All images supplied by the Nakuru Eye Study Group, regardless of quality, were sent for grading. No manipulation of the images was allowed while grading other than using grey-scale for viewing the images. All images were first categorized for quality as excellent, good, fair, borderline and ungradeable.

Interviews

Participants were interviewed by trained nurses. Information was collected on demographic data, education and asset ownership. People were asked whether their mother tongue was ''Kikuyu,'' ''Kalenjin'' or other, to assign ethnicity. Information was also collected on health behaviors (smoking, alcohol use) and health status (diagnosis of diabetes or hypertension, family history and their treatment).

Anthropometric Data Collection

A random finger-prick blood sample was taken to measure glucose (Accutrend GC system, Roche Diagnostics UK, Burgess Hill, UK) and cholesterol levels (Accutrend GC system). A nurse recorded the blood pressure of participants three times on the right arm of the participant, at least 5 minutes apart after an initial period of five minutes of rest using a digital automatic monitor (HEM907, Omron, Omron healthcare UK, Milton Keynes, UK). Weight was measured to the nearest kilogram using standard scales (Seca 761 scales, Seca, Birmingham, UK) after the participant had removed all heavy clothing and shoes. Height was measured to the nearest centimeter while the participant stood without shoes using a standardized stadiometer (Leicester Height Measure, Seca, Birmingham, UK). For weight and height, the average of two readings was recorded. Waist and hip circumferences were measured with a tape to the nearest centimeter.

Grading for DR

Grading for DR was undertaken for all participants with diabetes. The definitions used were as follows:

Non-proliferative DR (NPDR):

- SLB: Intra-retinal hemorrhages, microaneurysms venous beading, or prominent intra-retinal microvascular abnormality **and no** signs of proliferative retinopathy.

  Retinal images:
  - Mild: microaneurysms and retinal hemorrhages only were seen.
  - Moderate: In addition to microaneurysms, multiple deep, round or blot hemorrhages were noted.
  - Severe: Presence of features described before plus existence of vascular features such as venous loops, venous beading and intra-retinal microvascular abnormality.

Proliferative DR:

- SLB: Neovascularization and/or vitreous/pre-retinal hemorrhage.

  Retinal images:
  - New vessels on the disc new vessels elsewhere, pre-retinal or vitreous hemorrhage or pre-retinal fibrosis with or without tractional retinal detachment.

Macular edema:

- SLB: Retinal thickening or hard exudates in the posterior pole within 500 μm of the fovea.

  Retinal images:
  - Exudates within one disc diameter, the presence of circinate exudates within the macula and multiple hemorrhages within one disc diameter.

Clinically significant macular edema:

- SLB: Leakages involving or near the fovea.

  Retinal images:
  - Not assessed

All images were graded by the senior grader (IL). In case of difficulties, the adjudicator (TP) looked at the images. The adjudicator also looked at 5% of randomly selected images to ensure quality control. As diabetic macular edema is a stereo feature, clues seen on mono images were used. Data were entered onto Microsoft Excel and checked for consistency by a data monitor.

Data Entry and Analysis

A data entry package in EpiData software v2.1 (EpiData Association, Odense, Denmark) was developed for this study, which incorporated range checks. Data were double entered and consistency checks were performed each evening and inconsistencies corrected the same day.

The prevalence of DR and stages of DR were estimated, and the cluster design of the study was taken into account when calculating CIs around the prevalence estimates.

A continuous socioeconomic status (SES) score was produced for each participant using principle component analysis based on asset ownership, household type and education. The score was divided into quartiles to categorize the study participants into four socioeconomic groups with a higher score representing higher SES. Body mass index was calculated as height in meters/weight in kilograms^2.The clusters were defined as *rural* or *urban* according to the

classification used by the District Health Statistics office, Nakuru.[20] Diabetes was defined as per World Health Organization standards for population-based studies: reported current medication (tablets or insulin) or diet control for diabetes or random blood glucose level $\geq$11.1 mmol/L.[21]

Statistical analyses were undertaken using STATA version 10.0 (Stata Corp Inc, College Station, TX, USA). Logistic regression analyses were produced to assess the univariate associations between potential risk factors and prevalent DR among those with diabetes. Multivariable logistic regression models were developed through stepwise selection, with variables at the $p<0.05$ level retained.

Ethical Approval

Ethical approval for the study was granted by the London School of Hygiene & Tropical Medicine ethics committee and also Kenya Medical Research Institute. Approval was also granted by the Provincial Medical Officer Rift Valley and the Nakuru District Medical Officer of Health. Written approval was sought from the administrative heads in each cluster, usually the village chief. All participants gave written or verbal consent to participate. People requiring medical treatment were referred to the appropriate center. This research adhered to the guidelines of the Declaration of Helsinki.

RESULTS

A total of 5010 subjects were enumerated for this study. Of these, 4414 participants underwent examination to give a response rate of 88.1%. Of the non-respondents 584 (98%) were away working or visiting family outside the cluster location and 12 (2%) refused to participate.

Of the 4414 study participants, 4387 (99.4%) had a random blood sugar test for diabetes. A total of 244 people reported they had been previously diagnosed with diabetes mellitus and were labeled as ''known diabetes mellitus'' (5.6%). A further 43 had random blood sugar levels above 11.1 mmol/L and were thus labeled ''newly diagnosed diabetes mellitus'' (1.0%). The total number with definite diabetes mellitus was therefore 287 (6.5%). People with diabetes were less likely to be Kalenjin, compared to Kikuyu, were more likely to live in urban areas, and had higher education and SES scores than those without diabetes (Table 1). Those with diabetes were also more likely to be current smokers, and overweight. Among those ''known diabetes mellitus,'' 196 (80.3%) were receiving treatment. The time since diagnosis was 1–5 years for 126 people (51.6%), 6–10 years for 64 people (26.2%) and more than 10 years for 54 people (22.1%).

TABLE 1. Participant sociodemographic variables in relation to diabetes status, Nakaru district, Kenya.

	Diabetic *n* (%)	Non-diabetic *n* (%)	Age-, sex-adjusted OR (95% CI)
Age, years			
50–59	107 (37)	1825 (45)	Reference
60–69	103 (36)	1196 (29)	1.5 (1.1–1.9)
70–79	46 (16)	692 (17)	1.1 (0.8–1.6)
80+	31 (11)	387 (9)	1.4 (0.9–2.1)
Sex			
Male	139 (48)	1963 (48)	Reference
Female	148 (52)	2137 (52)	(0.8–1.3)
Language			
Kikuyu	221 (77)	2534 (62)	Reference
Kalenjin	25 (9)	987 (24)	0.3 (0.2–0.4)
Other	41 (14)	579 (14)	0.9 (0.6–1.2)
Location			
Urban	142 (49)	1292 (32)	2.3 (1.8–3.0)
Rural	145 (51)	2808 (68)	Reference
Education			
Any	222 (77)	2711 (66)	1.5 (1.3–1.7)
None	65 (23)	1389 (34)	Reference
SES score			
1 (poorest)	25 (9)	1067 (26)	Reference
2	41 (14)	1050 (26)	1.7 (1.0–2.8)
3	84 (30)	1008 (25)	3.9 (2.5–6.1)
4 (richest)	135 (47)	956 (23)	7.1 (4.6–10.9)
Smoking status			
Never	206 (72)	2861 (70)	Reference
Current	5 (2)	336 (8)	5.3 (2.1–13.2)
Former	75 (26)	892 (22)	1.1 (0.8–1.5)
Alcohol consumption			
Never	121 (42)	1582 (39)	Reference
Ever	166 (58)	2514 (61)	1.3 (1.0–1.7)
BMI Category			
Underweight	17 (6)	599 (15)	0.5 (0.3–0.9)
Normal	107 (38)	2064 (51)	Reference
Overweight	94 (33)	897 (22)	2.2 (1.6–2.9)
Obese	63 (22)	504 (12)	2.8 (2.0–3.9)

BMI, body mass index; CI, confidence interval; OR, odds ratio; SES, socioeconomic status

Of 4381 people who underwent ophthalmic examination (99.3%), all had slit lamp examination and 3387 had retinal photographs taken, of which 83 images were ungradable (2.5%). Among the 287 with definite diabetes mellitus, for 10 there was no view of the retina, and 195 had fundus photographs taken which could be graded in at least one eye (''diabetic image group''). For the remaining 82, DR was graded on the basis of SLB examinations only (''diabetic SLB group''). All subjects in the diabetic image group also had SLB.

PREVALENCE AND SEVERITY OF DR

The overall prevalence of any DR among the 195 patients with definite diabetes and with retinal images in the study population was 35.9% (95% CI 29.7–42.6%; Table 2). The most common grade of DR was

TABLE 2. Prevalence of diabetic retinopathy (DR) among diabetics in Nakaru district, Kenya, who underwent both slit lamp biomicroscopy (SLB) examination and had retinal images taken.

Category of DR	Retinal images		SLB		Prevalence ratio (image/SLB):
	n	Prevalence, % (95% CI)	*n*	Prevalence, % (95% CI)	
No DR[a]	125	64.1 (57.4–70.3)	153	78.4 (73.0–82.5)	
Mild/Moderate	43	22.1 (16.1–29.4)	26	13.3 (10.1–18.8)	1.6
Severe NPDR/PDR[b]	27	13.9 (10.0–18.8)	16	8.2 (5.0–12.4)	1.7
Any DR	70	35.9 (29.7–42.6)	42	21.5 (17.5–27.0)	1.6

[a]27 with mild NPDR and 1 with PDR graded as no DR by slit lamp
[b]16/17 with PDR correctly diagnosed while 10 with severe NPDR graded as mild/moderate NPDR by SLB.
CI, confidence interval; NPDR, non-proliferative diabetic retinopathy; PDR, proliferative diabetic retinopathy

TABLE 3. Sensitivity and specificity of diabetic retinopathy (DR) diagnosis by slit lamp biomicroscopy (SLB), Nakaru district, Kenya.

	Gold Standard: DR diagnosis by retinal imaging		
	Condition positive	Condition negative	
Test: DR diagnosis by SLB			
Test positive	42 (True positive)	0 (False positives)	Positive predictive value = 100%
Test negative	28 (False negatives)	125 (True negative)	Negative predictive value = 81.7%
	Sensitivity = 60.0%	Specificity = 100%	

TABLE 4. Prevalence of diabetic retinopathy (DR) among 277 diabetics with gradable retinas from Nakaru district, Kenya.

	Mild and moderate non-proliferative DR	Severe non-proliferative DR and proliferative DR	Any DR
DR confirmed by retinal images (A), *n*	43	27	70
DR confirmed by slit lamp only (B), *n*	11	6	17
Total DR, *n*	54	33	87
Correction factor	[A + (B × 1.6)]		
Adjusted total, *n*	61	37	97
Adjusted prevalence, % (95% CI)	22.0 (17.4–27.5)	13.4 (9.7–18.1)	35.0 (29.5–41.0)

CI, confidence interval

mild/moderate NPDR (22.1%, 95% CI 16.1–29.4%), while severe NPDR or proliferative DR were less frequent (13.9%, 95% CI 10.0–18.8%).

Among the 70 patients with DR, 65 (93%) had macular edema including eight with clinically significant macular edema (CSME). Macular edema was therefore present in 33.3% (95% CI 25.8–39.4%) of patients with diabetes, of which CSME was present in 4.1% (95% CI 1.9–8.2). Vision-threatening DR requiring immediate photocoagulation (i.e. those with CSME, severe NPDR or proliferative DR) was present in 28 of the 195 definite diabetics with retinal images, a prevalence of 13.4% (95% CI 9.6–16.3%).

SLB significantly under-diagnosed DR compared to retinal photography. This applied to all grades of DR. In total, all DR was under-diagnosed by SLB by a factor of 1.6. In comparison to gold standard grading by retinal images, grading of DR by SLB had low sensitivity (60%) but high specificity (100%; Table 3). Under-diagnosis of DR by SLB was therefore largely due to assigning a lesser grade to the severe NPDR and reporting no DR in many with mild NPDR. The one case with proliferative DR missed by SLB had new vessels at the disc as the only feature seen on images. There were no false positive cases.

A total of 87 diabetics had features of DR giving a prevalence of 31.4% (95% CI 26.3–37.0%; Table 4). Applying the correction factor of 1.6 for under diagnosis by SLB to the 17 diagnosed by SLB alone results in an adjusted estimate of 97 people with DR among the 277 diabetics with complete data, and an overall prevalence of DR of 35.0% (95% CI 29.5–41.0%) among those with diabetes.

The prevalence of all levels of VI was higher among the 87 participants with confirmed DR diagnosed (by images or SLB) compared to participants without DR (Table 5), and overall one in four people with DR had visual impairment (presenting VA < 6/12 in the better

TABLE 5. Visual impairment (VI) and diabetic retinopathy (DR) in Nakuru district, Kenya.

	People with DR ($N = 87$)		People without DR ($N = 4294$)	
Visual acuity	*n*	Prevalence, % (95% CI)	*n*	Prevalence, % (95% CI)
Normal, ≥6/12	64	73.6 (62.8–82.2)	3648	85.0 (83.8–86.0)
Mild VI, <6/12–6/18	5	5.7 (2.1–13.5)	219	5.1 (4.5–5.8)
Moderate VI, <6/18–6/60	13	14.9 (8.5–24.6)	343	8.0 (7.2–8.8)
Severe VI, <6/60–3/60	1	1.1 (0.06–7.1)	17	0.4 (0.2–0.6)
Blind, <3/60	4	4.6 (1.5–12.0)	67	1.6 (1.2–2.0)

CI, confidence interval

eye). VI among people with DR may be attributable to DR, cataract, refractive error or other causes. Among the 71 people who were blind in the Nakuru study (presenting VA < 3/60 in the better eye), four had DR (5.6%), to give a prevalence of DR blindness of 0.09% (95% CI 0.03–0.25%) in this population.

The results for the risk factor analyses were undertaken only on participants who had DR graded by retinal images, as case status could not be confirmed confidently for those with only SLB examination. The prevalence of DR was lower in the older age groups, but there was no clear association with sex or urban/rural residence (Table 6). The prevalence of DR was strongly associated with diabetes-related factors, including duration of diabetes, uncontrolled diabetes and treatment with insulin. Systemic factors were less clearly associated with DR: DR prevalence was higher among non-smokers and hypertensives, but there was no association with BMI. Education, tribe, SES, family history, waist-to-hip ratio, and cataract surgery were not associated with prevalence of DR (data not shown). In the multivariable analyses, the prevalence of DR remained associated with younger age, male sex, duration of diabetes, control of diabetes and compliance with treatment.

Seven individuals with diabetes in the survey population had undergone photocoagulation in the past; six in one eye only and one in both eyes. Among those who had received photocoagulation, three had undergone macular grid laser in one eye, one received both pan retinal and grid laser in both eyes and three underwent pan retinal laser in one eye. Among the seven who had evidence of laser treatment, five (71.4%) still had vision-threatening DR. Among those with vision-threatening DR, coverage of photocoagulation in those needing immediate laser was 25%; 24% in males and 27% in females (Table 7).

DISCUSSION

We undertook a large population-based survey of DR among people aged 50 years and older in Nakuru, Kenya. Prevalence of diabetes was 6.5%.[22] Among those with diabetes, the prevalence of DR was relatively high with more than one in three diabetics affected, though most DR was mild or moderate in severity. SLB substantially under-diagnosed DR in comparison to retinal photography, particularly for the milder grades of DR, although there were no false positives for DR by SLB. The prevalence of blindness or VI associated with DR was very low, likely due to the low prevalence of diabetes. Moreover, some of the cases of VI among people with DR may be attributable to cataract, refractive error or other causes, rather than DR. Logistic regression analyses indicated that the most important factors associated with DR were younger age, male sex and factors related to diabetes (e.g. duration and control of diabetes). The coverage of photocoagulation was very low.

A large systematic review of the epidemiology of DR and maculopathy in Africa identified 62 studies from 21 countries, including 3 surveys, 2 cohort studies, 5 case-control studies and 52 clinic-based studies.[23] Among the three population-based studies from Nigeria, Egypt and Mauritius, the reported prevalence of DR among diabetics ranged from 30.2–31.6%, and the prevalence of proliferative DR from 0.9–13%. The range of estimates for the clinic-based studies was much wider. Our findings for prevalence of DR are therefore closely aligned with these previous studies (35.9%, 95% CI 29.7–42.6%) although we find evidence for a higher prevalence of proliferative DR among diabetics (8.7%, 95% CI 5.7–13.1%) compared to those previously reported, but comparable to those reported in Caucasian populations.[24,25] Macula edema was present in 33.3% (95% CI 25.8–39.4%) of diabetics, of which CSME was present in 4.1% (95% CI 1.9–8.2%) of participants, similar to findings reported previously in other non-African populations.

The prevalence of diabetes is still relatively low in Africa, compared to other continents, however it is anticipated the prevalence will escalate over the coming decades.[4] Despite the relatively low prevalence of diabetes, the proportion of patients with DR was similar to that reported in other settings, and there was a clear need for treatment in this group to prevent the onset of blindness. Given that most of the diabetics in this sample were known to have the condition, the most parsimonious method for identifying those with sight-threatening DR needing treatment would be to screen those known to have the disease, rather than undertake population-based

TABLE 6. Association of risk factors and presence of diabetic retinopathy (DR; diagnosed by retinal imaging) among diabetics in Nakaru district, Kenya.

Variable	DR cases, *n*	Prevalence of DR, % (95% CI)	Age– and sex–adjusted OR (95% CI)	Multivariate–adjusted OR (95% CI)[a]
Age, years				
50–59	28	36.8 (26.9–48.1)	Reference	Reference
60–69	30	41.0 (30.3–52.8)	1.1 (0.6–2.2)	Reference
70–79	7	21.9 (11.9–36.8)	0.5 (0.2–1.3)	Reference
80+	5	23.8 (10.9–44.5)	0.5 (0.2–1.6)	0.4 (0.2–1.0)
Sex				
Male	44	38.6 (30.9–46.9)	Reference	Reference
Female	26	29.6 (20.6–40.4)	0.7 (0.4–1.3)	0.5 (0.2–1.0)
Location				
Rural	29	30.9 (23.4–39.5)	Reference	
Urban	41	38.0 (29.1–47.8)	1.3 (0.7–2.4)	
Diabetes case status				
Known diabetic	61	35.9 (28.7–43.9)	Reference	
Newly diagnosed	9	26.5 (13.4–45.6)	0.6 (0.3–1.4)	
Duration of diabetes, years				
0–5	28	23.3 (16.4–32.1)	Reference	Reference
6–10	20	47.6 (32.4–63.3)	3.1(1.4–6.9)	4.0(1.7–9.1)
>10	22	55.0 (41.2–68.1)	3.7(1.7–7.9)	4.4(1.9–10.2)
Blood glucose level, mmol/L				
≤11.1	29	27.4 (21.5–65.1)	Reference	Reference
>11.1	38	44.7 (29.1–65.4)	2.0 (1.1–3.7)	2.9 (1.3–6.9)
Treatment type				
Insulin	11	64.7 (40.7–83.05)	Reference	Reference
Oral	41	43.6 (32.7–55.2)	0.5 (0.2–1.6)	Reference
Diet only	4	23.5 (9.3–48.1)	0.2 (0.04–0.8)	Reference
Newly diagnosed	9	28.1 (14.4–47.7)	0.2 (0.1–0.8)	Reference
None	5	18.5 (7.7–38.4)	0.1 (0.03–0.5)	0.3 (0.1–0.8)
Smoking status				
Non smoker	49	36.0 (28.3–44.5)	Reference	Reference
Current	1	20.0 (4.2–58.7)	0.5 (0.04–5.0)	0.4 (0.2–1.0)
Former	20	32.8 (23.6–43.6)	0.6 (0.3–1.3)	
Hypertension				
Yes	58	37.9 (30.8–45.6)	1.9 (0.9–4.1)	
No	12	24.5 (15.3–36.8)	Reference	
BMI[b]				
Normal (18.5–24.9 kg/m^2)	28	37.3 (28.1–47.6)	Reference	
Overweight (25–29.9 kg/m^2)	27	37.5 (25.2–51.7)	1.3 (0.7–2.7)	
Obese (>30 kg/m^2)	15	34.1 (24.–45.9)	1.1 (0.5–2.4)	

[a]Adjusted for age, sex, duration of diabetes, blood glucose levels, treatment for diabetes, smoking, and visual impairment.
[b]None underweight
BMI, body mass index; CI, confidence interval; OR, odds ratio

screening for DR at this stage. The under-diagnosis of DR by SLB is of concern, given the lack of availability of retinal photography and grading in Africa. However, it is encouraging to note that all but one case of sight-threatening DR were identified by slit lamp examination and that it was mainly early DR cases that were missed. Given the low availability of retinal photography and grading in Africa, screening by slit lamp examination may still be a viable screening option for detecting cases needing treatment provided that the screener is adequately trained.

There were a number of limitations to this study. Blood glucose measures were obtained from non-fasting blood samples, rather than through use of an oral glucose tolerance test or fasting blood glucose. We may therefore have under-diagnosed diabetes, and consequently underestimated the prevalence of DR in this population. Detailed ophthalmic examinations were conducted, including assessment of DR by the gold standard method of retinal photography with grading of images by a high quality grading center. However, not all participants with diabetes in the sample had DR graded by imaging (70% overall) due to technical issues with moving the camera. Furthermore, a few of the images were ungradable. Since it is likely that most of the images that could not be graded were due to cataract, and cataract is related to diabetes, this bias may have led to an underestimation of the prevalence of DR in the population, although any effect is likely to have been small.

TABLE 7. Diabetes, diabetic retinopathy (DR) and laser coverage by sex, Nakaru district, Kenya.

	Male	Female	Total
Diabetes with gradable retina, *n*	112	83	195
Diabetes with DR[a], *n*	50	37	87
People needing immediate laser treatment[b], *n*	17	11	28
Eyes needing immediate laser treatment[b], *n*	34	22	56
Received photocoagulation, people (met need), *n*	4	3	7
Received photocoagulation, eyes (met need), *n*	5	3	8
Laser coverage, people: Met need/total need, %	23.5	27.2	25.0
Laser coverage, eyes: Met need/total need, %	14.7	13.6	14.3

[a]DR diagnosis through slit lamp biomicroscopy or retinal image
[b]Vision-threatening DR

Macular edema traditionally has stereo definitions, however, we only had mono images, therefore clues from these had to be used to establish the potential presence of macular edema. Macular edema was graded using surrogate markers, such as exudate within one disc diameter, circinate within the macula and multiple hemorrhages within one disc diameter. There was no way of determining if there was subtle macular edema that would have required the presence of stereo images, therefore macular edema without the presence of exudates and multiple hemorrhages could have been missed. For SLB, CSME assessment did not include assessment of ''one or more disc diameters of retinal thickening, part of which is within one disc diameter of the macular center'' and so may have missed some cases leading to an underestimation of prevalence. The study included only people aged 50 years and older, and so the estimated prevalence of DR will not be generalizable to the entire population. However, a recent survey in Kenya confirmed that diabetes is relatively rare before middle age,[26] so that focusing on the age group 50+ years would capture the vast majority of cases with DR in the population, given the strong association between duration of diabetes and the development of DR. In terms of strengths, the sample was large, and included both rural and urban participants. There was a high response rate, and the sample was representative across Nakuru, limiting the impact of selection bias. Detailed lifestyle and anthropometric data were collected.

In conclusion, DR remains a threat to the sight of those with diabetes in this elderly Kenyan population, despite the overall low prevalence of diabetes. Screening for DR in those subjects known to have diabetes may enable timely identification of those requiring treatment, potentially resulting in prevention of sight loss.

DECLARATION OF INTEREST

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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Prevalence of Age-Related Macular Degeneration in Nakuru, Kenya: A Cross-Sectional Population-Based Study

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Abstract

Background: Diseases of the posterior segment of the eye, including age-related macular degeneration (AMD), have recently been recognised as the leading or second leading cause of blindness in several African countries. However, prevalence of AMD alone has not been assessed. We hypothesized that AMD is an important cause of visual impairment among elderly people in Nakuru, Kenya, and therefore sought to assess the prevalence and predictors of AMD in a diverse adult Kenyan population.

Methods and Findings: In a population-based cross-sectional survey in the Nakuru District of Kenya, 100 clusters of 50 people 50 y of age or older were selected by probability-proportional-to-size sampling between 26 January 2007 and 11 November 2008. Households within clusters were selected through compact segment sampling. All participants underwent a standardised interview and comprehensive eye examination, including dilated slit lamp examination by an ophthalmologist and digital retinal photography. Images were graded for the presence and severity of AMD lesions following a modified version of the International Classification and Grading System for Age-Related Maculopathy. Comparison was made between slit lamp biomicroscopy (SLB) and photographic grading. Of 4,381 participants, fundus photographs were gradable for 3,304 persons (75.4%), and SLB was completed for 4,312 (98%). Early and late AMD prevalence were 11.2% and 1.2%, respectively, among participants graded on images. Prevalence of AMD by SLB was 6.7% and 0.7% for early and late AMD, respectively. SLB underdiagnosed AMD relative to photographic grading by a factor of 1.7. After controlling for age, women had a higher prevalence of early AMD than men (odds ratio 1.5; 95% CI, 1.2–1.9). Overall prevalence rose significantly with each decade of age. We estimate that, in Kenya, 283,900 to 362,800 people 50 y and older have early AMD and 25,200 to 50,500 have late AMD, based on population estimates in 2007.

Conclusions: AMD is an important cause of visual impairment and blindness in Kenya. Greater availability of low vision services and ophthalmologist training in diagnosis and treatment of AMD would be appropriate next steps.

Please see later in the article for the Editors' Summary.

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Abbreviations: AMD, age-related macular degeneration; SES, socioeconomic status; SLB, slit lamp biomicroscopy.

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Introduction

In the latest estimates of global blindness and visual impairment undertaken by the World Health Organization, in 2010, age-related macular degeneration (AMD) is the third most common cause of blindness worldwide behind cataracts and glaucoma [1]. It has remained an important cause of blindness globally since the last World Health Organization survey in 2002, in which it was identified as the leading cause of blindness in high-income countries [2]. As the global population ages, AMD is likely to increase in importance. Currently, no curative treatment exists. The recent promise of anti–vascular endothelial growth factor treatments is unlikely to offset the growth of AMD globally, as these treatments are only useful in exudative AMD and are not currently widely accessible outside of high-income countries. Nutritional interventions can reduce the progression of certain subtypes of early AMD [3]; however, protective levels of required vitamins and minerals are difficult to obtain in a healthy diet, and the cost of supplementation is prohibitive for many who could potentially benefit [4].

The majority of data on AMD available globally is from population-based studies undertaken in white and Asian populations [5–13], and few data are from peoples of African descent. The data that do exist for individuals of African descent are largely from studies undertaken in populations living outside of the African continent [14,15]. It is presumed that AMD is rare in Africans; however, in the last 10 y, African population-based studies have suggested that posterior segment eye diseases are highly prevalent, and this group of disorders, which includes AMD, diabetic retinopathy, and glaucoma, has been highlighted as either the leading or second leading cause of blindness in surveys undertaken in Cameroon [16], Tanzania [17], Kenya

[18], Rwanda [19], Zanzibar [20], and Guinea [21]. These studies, however, did not assess AMD as a specific entity and did not use digital retinal photography. Moreover, comparative data for whites and Africans living in the same geographical area (Baltimore, Maryland, US) have suggested differing predispositions towards AMD, with possible genetically protective factors for AMD progression in individuals of African descent compared to their white counterparts [22]. Population-based evidence for African populations living in Africa on the prevalence of the disease, and of the risk factors for AMD, is therefore important.

The purpose of this study was to estimate the prevalence and risk factors for AMD in the age group 50 y and over in an African population in Nakuru District, Kenya, using digital retinal photography and slit lamp biomicroscopy (SLB). Nakuru District is within the Rift Valley Province in Kenya, with a population of nearly 10 million, approximately one-quarter of the Kenyan population. Nakuru is diverse in its ethnic mix (all 42 tribes present in Kenya represented within the district), range of socioeconomic activity, and urban/rural mix.

Methods

Ethics Statement

Ethical approval was granted by the London School of Hygiene & Tropical Medicine Ethics Committee and by the Kenya Medical Research Institute. Approval was also granted by the Rift Valley Provincial Medical Officer and the Nakuru District Medical Officer of Health. Written approval was sought from the administrative head in each cluster, usually the village chief. All participants gave written or verbal consent to participate. People requiring medical treatment were referred to the appropriate centre.

Sampling Strategy and Recruitment

The study fieldwork was carried out in two phases, from 11 January to 2 June 2007 and from 8 April to 11 November 2008.

Recent census data for Kenya were not available [23], and therefore election roll lists that were renewed in 2006 in preparation for the 2007 general elections were used as the sampling frame for this survey. 100 clusters were selected with a probability proportional to the size of the population. A cluster was defined as the area served by a polling station.

Households were selected within clusters using a modified compact segment sampling method [24]. Each cluster was divided into segments so that each segment included approximately 50 people aged $\geq$50 y. One segment was selected at random, and all eligible people were included sequentially until 50 had been examined. Location data including GPS coordinates of houses and mobile phone contacts were taken to allow follow-up of all those examined.

This sample size was sufficient to estimate a prevalence of AMD of 3.0% among those aged 50+ y, with a required precision of 0.5%, 95% confidence, a design effect to account for clustering of 1.5, and a response rate of 90% (Epi Info 6.04, US Centers for Disease Control and Prevention).

Ophthalmic and General Examination

Suitable predetermined examination sites were selected, on the recommendation of the village leader, with close proximity to the cluster and to electricity supply (mains or generator).

Visual Acuity

The presenting visual acuity was defined as the number of letters read correctly without glasses if the participant did not have glasses or with glasses if they had them. Testing was done on each eye separately at 4 m using a reduced LogMAR tumbling "E" chart [25] in a well-illuminated area, as described elsewhere [26].

Fundus Photography

The participants had two nonstereoscopic digital 45° fundus photographs taken per eye by an ophthalmic clinical officer using a TRC-NW6S Non-Mydriatic Retinal Camera with a ten-megapixel Nikon D80 camera (Topcon). One image was centred on the optic disc, while the other was centred on the macula. The digital images were stored on hard disc, backed up on an external drive, and one copy saved on CD was forwarded to the Retinal Grading Centre at Moorfields Eye Hospital Reading Centre in London for grading and confirming the clinical diagnosis of posterior segment disease.

Image Grading

The senior grader (I. L.) graded all images. All images were first categorised for quality as excellent, good, fair, borderline, or ungradable. All questionable lesions and all eyes classified as having late-stage AMD were adjudicated by the Moorfields Eye Hospital Reading Centre clinician (T. P.). Any lesions considered to be due to other causes such as myopia and inflammatory disease were not graded for AMD, and these were also verified by T. P. The adjudicator also graded 5% of randomly selected images to ensure quality control. Data were entered into Excel and checked for consistency by a data monitor. Those with images were classified as "image group" for further analysis.

Retinal Examination

SLB was performed after pharmacological dilatation with guttae tropicamide 1% using a 90 diopter lens. Assessment was inclusive of the macula, the retinal vasculature, and the peripheral retina. The view of the retina was recorded as clear, hazy, or no view. The macula was examined for presence of drusen, hypo- or hyper-pigmentation, dry AMD or geographic atrophy (GA), and neovascular changes. Any other pathologies of the retina or vitreous, e.g., retinal detachments or vitreous haemorrhages, were also noted, and a description given. Those with slit lamp examination were classified as "SLB group".

Definitions Used

A modified version of the International Classification and Grading System for Age-Related Maculopathy and Age-Related Macular Degeneration [27] was used for image grading. Drusen were categorised based on size, uniformity of colour, and margins. Based on these, patients were classified into hard or soft drusen categories. Small drusen, less than 63 μm, were considered to be hard. Large drusen with a uniform density, sharp margins, and a nodular surface texture were placed in the soft distinct category, whereas those without sharp margins were classified as indistinct. Where end-stage disease was apparent, patients were classified as having geographic atrophy if there were well-demarcated regions with diameters in excess of 175 μm, within which large choridal vessels were clearly visible, owing to the atrophy of the overlying choriocapillaris and retinal pigment epithelium. Neovascular AMD was graded as present when exudative features, such as serous fluid, haemorrhage, lipid exudates, or fibrosis, were seen to be originating primarily from the subretinal and pigmentepithelial tissue layers.

SLB grading of AMD was as follows: (1) drusen present: presence of discrete whitish-yellow spots at the macula area; (2) pigmentary changes present: presence of increased pigment or

hyperpigmentation or sharply demarcated areas of depigmentation or hypopigmentation of the retinal pigment epithelium; (3) dry AMD or geographic atrophy: atrophy of the retinal pigment epithelium, with visible underlying choroidal vessels; (4) wet or neovascular AMD: presence of retinal pigment epithelium detachment, subretinal or subpigment epithelial neovascularization, or fibrous scar tissue, haemorrhages, or exudates; (5) no AMD: none of the features described above were present; (6) cannot assess: the retina could not be adequately visualised for grading. Case definitions were based on the eye with more severe status if both eyes were gradable, and on the gradable eye if only one eye was gradable ($n = 37$).

Detailed interviews were undertaken in the local language covering demographic details, information on risk factors, socioeconomic status (SES), and full past medical history. SES was evaluated using a continuous asset score that was produced for each participant using a scoring system derived through principal component analysis in an earlier study in this setting [28,29]. The scale included assessment of 17 context-specific asset items owned by the household, including different types of furniture, electrical equipment, cattle, and vehicles. Information was collected on five household characteristics, including the building material of the floor, roof, and walls; type of toilet; and the number of rooms. The score was divided into quartiles based on the distribution across all the study participants, to derive a measure of relative SES.

Weight, height, waist and hip circumference, blood pressure, and random cholesterol and glucose blood levels were also measured. "Mother tongue" was used as a measure of tribal affiliation.

Data Handling and Statistical Analysis Methods

Data entry. Data were double-entered into a specially developed dataset (EpiData Entry, version 2.1). Consistency checks were performed each evening, and inconsistencies corrected the same day.

Data analysis. The prevalence of AMD was estimated, and the "svy" command in Stata was used with a design effect of 1.5 in order to take into account the cluster sampling survey methodology when calculating confidence intervals around the prevalence estimates.

Statistical analyses were undertaken using Stata. Logistic regression analyses were produced to assess the univariate associations between potential risk factors (age, gender, SES, tribal origin, hypertension, diabetes, angina, cholesterol level, body mass index, waist:hip ratio, previous cataract surgery, smoking and alcohol consumption, education, and urban versus rural) and prevalent AMD. Multivariable logistic regression models were developed through stepwise selection, with variables retained at the $p<0.05$ level. These analyses were restricted to cases defined from the image group data, since definite disease status was available only for this group.

The data for individuals with both SLB and retinal images were used to calculate a correction factor (if needed) to apply to the SLB group to estimate the overall prevalence of AMD for Nakuru.

Estimated numbers of individuals within Kenya with AMD were extrapolated from population data from the US Census Bureau International Data Base (http://www.census.gov/population/international/data/idb/country.php) by applying age- and sex-specific prevalence estimates for the Kenyan population.

Results

There were 5,010 eligible individuals identified for this study. Of these, 4,414 participants underwent examination, giving a response rate of 88.1%, and 4,381 had full ophthalmic examination; 33 participants were not included in the ophthalmic analysis because of missing data as a consequence of equipment failure. Of the non-respondents, 584 (98%) were away working or visiting family outside the cluster location, and 12 (2%) refused to participate; none were excluded as a result of inability to communicate. The socio-demographic characteristics of the participant group are described in earlier publications [30]. Out of the 4,381 individuals who had ophthalmic examinations in the Nakuru study, 4,312 (98.4%) were successfully screened for AMD by SLB of the retina (SLB group).

3,387 (77.3%) participants underwent retinal photography. An image for grading for AMD in at least one eye was available for 3,304 individuals (75.4%) (image group). 3,274 individuals (74.7%) had both methods of screening (Figure 1).

Compared to people in the SLB group, those who had images taken were more likely to be male, younger, urban residents, not Kikuyu, not diabetic, and not visually impaired (Tables 1 and S1). A correction factor was necessary because there were significant differences in the characteristics of the SLB-only group compared to the image group, and so it was not possible to generalise the results from the image group to the whole population.

The prevalences of drusen and pigmentary irregularities as observed on the fundus images, by gender and age, are shown in Table 2. Note that varying features of AMD, e.g., drusen and pigmentation, can co-exist in a single eye and in both eyes and therefore one individual may be listed under more than one AMD characteristic. However, the prevalence of AMD in the population is based on the grading of AMD in a person. Drusen were present in a large proportion of the population. The most common type of drusen encountered in all ages was small, hard drusen, <63 μm, which were present in 59.1% of the study population. Large, soft drusen, which are considered to be indicative of early AMD, were present in 9.4% of the population. There were significant age trends (X^2 trend test, $p<0.001$), with increased prevalence of all drusen and all pigmentary changes from age 50 y to age 79 y. The gender difference was less strong, though drusen and pigmentary changes were more common in women than men. The overall prevalence of retinal pigment abnormalities was 4.8% (95% CI, 3.7–6.1). Increased pigment was seen more frequently than depigmentation in all age groups, and prevalence increased from 1.6% in the lowest age groups to 7.2% in those aged 80 y or more. The difference in prevalence of pigment in men and women was not significant ($p = 0.66$).

Neovascular AMD was more common (0.9%) than geographic atrophy (0.5%) (Table 3). There were significant age trends for both, with geographic atrophy being prevalent in only 0.3% of those in their 50 s and increasing to 2.0% in those age 80 y and over.

The prevalence of all stages of AMD was lower when SLB grading was used than when grading was from retinal images (Table 4). The total prevalence of AMD from SLB was 7.4% (early AMD, 6.7%, and late AMD, 0.7%), while the prevalence of AMD by retinal image grading was 12.4% (early AMD, 11.2%, and late AMD, 1.2%). A smaller proportion of participants were classified as ungradable by SLB (30; 1.6%) than by retinal image grading (83; 2.6%). A correction factor of 1.7 for total AMD needs to be applied for those who did not have retinal imaging (considered the gold standard) to get the true prevalence estimate of AMD in the SLB group.

Sensitivity and specificity analysis for the detection of early AMD and late AMD by SLB grading versus retinal imaging, in those individuals who had both SLB and image grading available, showed that SLB grading had poor sensitivity (early, 21.3%, and late, 36.8%) and good specificity (early, 95.2%, and late, 99.9%).

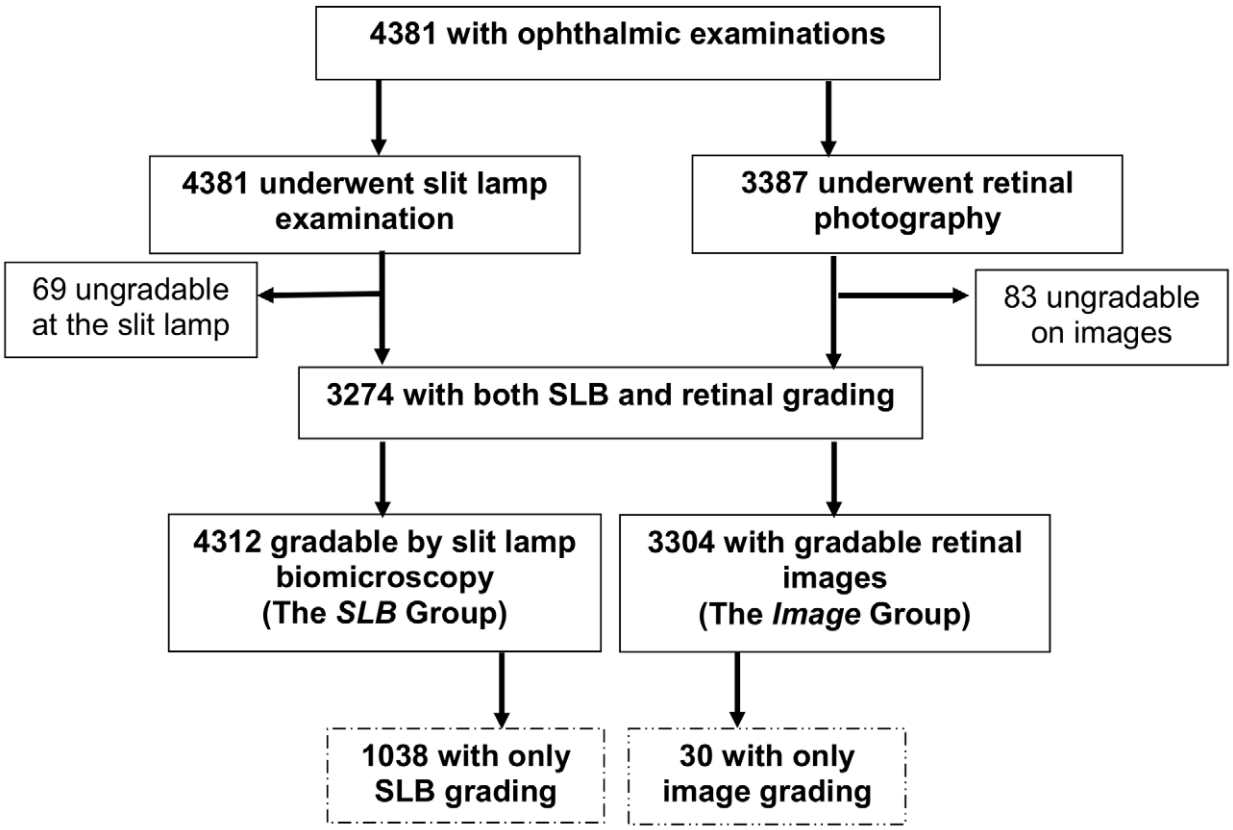

Figure 1. AMD study participation chart.
doi:10.1371/journal.pmed.1001393.g001

A total of 404 (366 early AMD and 38 late AMD) cases were confirmed by images, while another 85 cases (75 early AMD and ten late AMD) were detected in the group that received SLB only. Combining all cases gives a total of 489 cases, or a prevalence of 11.3% for AMD (435 [10.2%] early AMD and 48 [1.1%] late AMD) in this population. However, since SLB underdiagnosed AMD by a factor of 1.7, if this factor is applied to the SLB prevalences, an adjusted prevalence of 12.7% (11.4% for early AMD and 1.3% for late AMD) is reached (Table 5).

When extrapolating these data to the entire Kenyan population based on data from 2007, we estimated that there are 283,900 to 362,800 people over 50 y in Kenya with early AMD and 25,200 to 50,500 with late AMD.

Age/sex-adjusted analyses show that only age and gender were significantly associated with early AMD, with those affected more likely to be female and with prevalence increasing with each decade of age (Table 6).

Modelling age as a continuous variable did not alter the findings (Table S2).

Age/sex-adjusted analyses showed that only age was significantly associated with late AMD, with increased late AMD prevalence with every decade after 50 y (Table 7). All other variables showed no association.

Of the 487 people with any grade of AMD (diagnosed by SLB or retinal images), a total of 137 (28.1%) were visually impaired, including 12 blind people (2.5%; 95% CI, 1.3–4.8), four with severe visual impairment (0.8%; 0.3–2.2), and 82 with moderate visual impairment (16.8%; 13.4–20.9). 350 (71.9%; 7.0–76.4) of those with AMD had normal vision (Table 8). Among the 669 people with visual impairment in the entire Nakuru study, 137 (20.5%) had features of AMD, either exclusively or in combination with other pathology.

28 people had visual impairment due to AMD alone (i.e., no other visually impairing pathology found), a prevalence of 0.6% (95% CI, 0.4–1.0) for visual impairment from AMD in the population. 9.9% (seven of 71 people) of blindness in this survey was attributable to AMD.

Discussion

The prevalences of early and late AMD in this African population over 50 y of age were 11.2% and 1.2%, respectively.

Very few data exist on the prevalence and causes of AMD in Africa, and to our knowledge, this is the only population-based study in Africa using an internationally recognised grading system and digital retinal photographs. Although data from Rapid Assessment of Avoidable Blindness surveys exist, these cluster AMD with other posterior segment eye diseases, and so no direct comparisons can be made with the findings from this study. A Nigerian survey used similar methodology, including a population-based approach and fundus photographs; however, retinal imaging was performed only in individuals with a visual acuity

Table 1. Demographic characteristics of study participants ($n = 4,381$).

Attribute	Number (Percent) of Those with Grading by Retinal Images, $n = 3,304$	Number (Percent of Those with Only SLB Diagnoses, $n = 1,038$	Age- and Sex-Adjusted Odds Ratio (95% CI)
Gender			
Male	1,629 (49%)	450 (43%)	Baseline
Female	1,675 (51%)	588 (57%)	0.8 (0.7–0.9)
Age			
50–59 y	1,508 (78.0%)	426 (22.0%)	Baseline
60–69 y	997 (77.3%)	292 (22.7%)	1.0 (0.8–1.2)
70–79 y	547 (75.8%)	175 (24.2%)	0.9 (0.8–1.2)
80+ y	252 (63.5%)	145 (36.5%)	0.6 (0.4–0.7)
Environment			
Rural	2,143 (69%)	774 (75%)	Baseline
Urban	1,161 (31%)	264 (25%)	1.5 (1.3–1.7)
SES			
Poorest	783 (24%)	287 (27%)	Baseline
2nd quartile	815 (25 %)	267 (26%)	1.0 (0.9–1.2)
3rd quartile	840 (26%)	243 (23%)	1.1 (0.9–1.4)
Least poor	829 (25%)	252 (24%)	1.1 (0.9–1.3)
Tribe			
Kikuyu	1,997 (60%)	721 (70%)	Baseline
Kalenjin	780 (24%)	211 (20%)	1.3 (1.1–1.6)
Other	527 (16%)	106 (10%)	1.7 (1.3–2.1)
Diabetes			
Non-diabetic	3,091 (94%)	947 (92%)	Baseline
Diabetic	192 (6%)	86 (8%)	0.7 (0.5–0.9)
Visual impairment			
≥6/12	2,891 (88%)	820 (79%)	Baseline
<6/12	3,973 (12%)	218 (21%)	0.5 (0.4–0.6)

doi:10.1371/journal.pmed.1001393.t001

Table 2. Number and prevalence of features of early AMD (image group) and age-related maculopathy by sex and age ($n = 3,304$).

Attribute	Small Drusen (<63 μm)		Large Drusen (≥63 μm)		Hypopigmentation		Hyperpigmentation	
	N	Percent (95% CI)	*N*	Percent (95% CI)	*N*	Percent (95% CI)	*N*	Percent (95% CI)
Total	1,954	59.1 (56.1–62.1)	310	9.4 (8.2–10.7)	79	2.4 (1.7–3.3)	117	3.5 (2.7–4.6)
Age								
50–59 y	813	53.9 (50.0–57.8)	52	3.5 (2.6–4.6)	31	2.1 (1.2–3.4)	24	1.6 (0.9–2.7)
60–69 y	603	60.4 (56.4–64.3)	92	9.2 (7.5–11.4)	26	2.6 (1.7–4.1)	41	4.1 (2.8–6.0)
70–79 y	372	68.0 (63.6–72.2)	103	18.8 (15.4–22.9)	17	3.1 (1.8–5.4)	34	6.2 (4.3–8.9)
80+ y	166	66.1 (59.0–72.6)	63	25.1 (20.1–30.9)	5	2.0 (0.7–5.3)	18	7.2 (4.2–12.1)
***p*-Value[a]**	<0.001	<0.001	<0.001	<0.001				
Gender								
Male	889	54.6 (51.0–58.1)	123	7.6 (6.4–8.9)	36	2.2 (1.5–3.2)	45	2.8 (2.0–3.9)
Female	1,065	63.6 (60.0–67.1)	187	11.2 (9.3–13.4)	43	2.6 (1.7–3.9)	72	4.3 (3.1–5.9)
***p*-Value[b]**	<0.001	0.002	0.74	0.05				

[a]X^2 trend test for age groups.
[b]X^2 trend for sex differences.
doi:10.1371/journal.pmed.1001393.t002

Table 3. Number and prevalence of features of late AMD (image group) by sex and age ($n = 3,304$).

Attribute	Neovascular AMD		GA		No Late AMD	
	N	Percent (95% CI)	*N*	Percent (95% CI)	*N*	Percent (95% CI)
Total	29	0.9 (0.5–1.4)	18	0.5 (0.3–0.9)	3,266	98.9 (98.3–99.2)
Age						
50–59 y	5	0.3 (0.1–0.9)	3	0.2 (0.1–0.6)	1,503	99.5(99.0–99.8)
60–69 y	10	1.0 (0.5–2.0)	4	0.4 (0.2–1.1)	987	98.8 (97.8–99.8)
70–79 y	7	1.3 (0.6–2.9)	6	1.1 (0.4–2.8)	540	98.2 (96.3–99.1)
80+ y	7	2.1 (1.1–6.8)	5	2.1 (0.8–4.6)	246	96.4 (92.5–98.3)
***p*-Value[a]**	<0.001	<0.001	<0.001			
Gender						
Male	10	0.6 (0.3–1.2)	10	0.6 (0.3–1.2)	1,614	99.1 (95.7–97.5)
Female	19	1.1 (0.7–1.9)	8	0.5 (0.2–0.9)	1,652	98.6 (95.2–97.0)
***p*-Value[a]**	0.70	0.80	0.30			

[a]The features of late AMD, i.e., neovascular changes and geographic atrophy, are not mutually exclusive, so individuals may appear in both columns. The data for late AMD, and hence for "no late AMD", is person-specific and therefore mutually exclusive. Those with both GA and neovascular AMD are counted in the neovascular AMD group.

Table 4. Comparison of SLB and image groups.

Variable	Prevalence in Image Group	Prevalence in Same People by SLB	Underdiagnosis Factor for SLB
Number gradable	3,304	3,274	
Early AMD	366 (11.1%)	219 (6.7%)	1.7
Late AMD	38 (1.2%)	24 (0.7%)	1.6
Total AMD	404 (12.2%)	243 (7.4%)	1.7

Data are given as number (percentage).
doi:10.1371/journal.pmed.1001393.t004

Table 5. Determination of all AMD cases and adjusted prevalence including diagnosis by SLB.

Terms	Early AMD	Late AMD	Total AMD	No AMD
Confirmed by retinal images (*A*) ($n = 3,304$)	366	38	404	2,900
Confirmed only by SLB (*B*) ($n = 4,312$)	75	10	85	953
Total observed cases ($n = 4,342$)	441	48	489	3853
Prevalence	10.2%	1.1%	11.3%	88.7%
95% CI	(9.0–11.5)	(0.8–1.6)	(10.0–12.7)	(87.3–90.0)
Corrected prevalence (A+[$B \times 1.7$ or 1.6])/3,797	11.4%	1.3%	12.7%	87.4%

doi:10.1371/journal.pmed.1001393.t005

Table 6. Risk factors for early AMD.

Category	Risk Factor	Number with Early AMD	Prevalence (95% CI)	Age- and Sex-Adjusted Odds Ratio (95% CI)
Demographic factors	**Age group (years)**			
	50–59	82	5.5% (4.2–7.1)	Reference
	60–69	115	11.7% (9.8–13.9)	2.3 (1.7–3.1)
	70–79	110	20.5% (16.7–24.9)	4.7 (3.5–6.4)
	≥80	59	24.3% (19.3–30.1)	5.7 (3.9–8.3)
	Gender			
	Female	212	9.5% (7.7–10.6)	1.5 (1.2–1.9)
	Male	154	12.8% (10.6–15.5)	Reference
	Tribe			
	Kikuyu	244	12.3% (10.3–14.8)	Reference
	Kalenjin	80	10.4% (8.5–12.8)	0.8 (0.6–1.1)
	Other	42	7.8% (5.8–11.2)	0.9 (0.7–1.3)
	SES			
	1st quartile (poorest)	112	14.6% (12.2–17.4)	Reference
	2nd quartile	102	12.6% (10.0–15.8)	1.0 (0.7–1.3)
	3rd quartile	84	10.1% (8.0–12.7)	0.9 (0.7–1.2)
	4th quartile (richest)	65	7.9% (5.8–10.8)	0.8 (0.5–1.1)
Systemic factors	**Body mass index**			
	<25 kg/m2	252	12.2% (10.6–14.0)	Reference
	Overweight (25–29.9 kg/m2)	78	10.5% (8.3–13.1)	1.0 (0.7–1.3)
	Obese (≥30.0 kg/m2)	33	7.8% (5.2–11.4)	0.7(0.5–1.0)
	Diabetes			
	Yes	15	7.9% (4.3–14.1)	0.7 (0.4–1.1)
	No	350	11.5% (9.9–13.2)	Reference
	Hypertension			
	Hypertensive	213	12.8% (10.7–15.2)	1.2 (1.0–1.5)
	Non-hypertensive	152	9.7% (8.2–11.4)	Reference
	Angina grade			
	None	290	10.8% (8.7–11.9)	Reference
	Grade 1	55	12.4% (9.3–15.2)	1.2 (0.9–1.7)
	Grade 2	20	16.4% (11.5–22.8)	1.7 (1.0–2.9)
	Smoking			
	Current	21	7.8% (5.3–11.2)	0.8 (0.5–1.4)
	Former	77	10.5% (8.5–12.9)	1.0 (0.7–1.4)
	Never	267	11.9% (10.1–14.0)	Reference
	Alcohol			
	Current	68	11.6% (9.0–14.7)	1.3 (0.9–1.9)
	Former	160	11.3% (9.6–13.2)	1.0 (0.8–1.3)
	Never	137	11.1% (8.7–14.1)	Reference
Ocular features	**Cataract surgery**			
	Yes	26	15.2% (10.6–21.3)	0.9 (0.5–1.3)
	No	339	11.0% (9.5–12.7)	Reference

doi:10.1371/journal.pmed.1001393.t006

of ≤6/12 [26]. In the present study, 75.1% of individuals identified as having AMD had an acuity of 6/12 or greater.

Only one other prospective study of AMD in Africa was found in the peer-reviewed literature. A hospital-based study in South Africa that looked specifically at AMD in Africans was published in 1978 [31]. The study participants were aged 50 y and older, as in this study, and were examined by indirect ophthalmoscopy as well as photography. Higher levels of "senile macular degeneration", as AMD was then termed, were reported than in this study, affecting 17.4% of participants in the study. It is likely that the

Table 7. Risk factors for late AMD.

Category	Risk Factor	Number with Late AMD	Prevalence (95% CI)	Age- and Sex- Adjusted Odds Ratio (95% CI)
Demographic factors	**Age group (years)**			
	50–59	7	0.5% (0.2–1.0)	Reference
	60–69	12	1.2% (0.7–2.2)	2.8 (1.1–7.3)
	70–79	10	1.8% (0.9–3.7)	5.1 (1.9–13.5)
	≥80	9	3.6% (1.7–7.5)	10.4 (3.8–28.2)
	Gender			
	Female	23	1.0% (0.6–1.7)	1.8 (0.9–3.4)
	Male	15	1.6% (1.0–2.4)	Reference
	Tribe			
	Kikuyu	20	1.1% (0.6–2.1)	Reference
	Kalenjin	11	1.5% (0.8–3.1)	1.4 (0.7–3.0)
	Other	7	1.4% (0.7–3.2)	2.2 (0.9–5.5)
	Environment			
	Rural	31	1.6% (1.0–2.6)	Reference
	Urban	7	0.7% (0.3–1.45)	0.6 (0.2–1.3)
Systemic factors	**Cholesterol**			
	Low	31	1.1% (0.7–1.8)	Reference
	High	4	3.7% (1.4–9.6)	3.0 (1.0–8.9)
	Smoking			
	Current	4	1.6% (0.6–4.1)	2.2 (0.7–6.6)
	Former	6	0.9% (0.4–2.0)	1.0 (0.4–2.7)
	Never	28	1.4% (0.9–2.1)	Reference
	Alcohol			
	Current	7	1.3% (0.6–3.0)	0.9 (0.3–2.4)
	Former	12	0.9% (0.5–1.8)	0.5 (0.2–1.1)
	Never	19	1.7% (1.1–2.7)	Reference
Ocular features	**Cataract surgery**			
	Yes	6	4.0% (1.9–8.1)	2.1 (0.8–5.2)
	No	32	1.2% (0.7–1.8)	Reference

doi:10.1371/journal.pmed.1001393.t007

hospital population sampled was not representative of the general population, as enrolled participants had attended the hospital eye clinic of their own volition and therefore were more likely to have had symptomatic vision loss than the general population. Typically, the demographic of individuals attending a hospital clinic also differs from the general population in terms of SES and life expectancy. No population-based studies specifically reporting AMD in Africa have been published, to our knowledge.

The prevalence of AMD in this study was also lower than that in a study in the Caribbean, where a 28.7% prevalence of AMD was found [32]. In general, the prevalences in our study are similar to or higher than those documented for Hispanic and Asian populations (range 7.1%–13.6%) [13,33–36], but lower than those found in white populations (range 9.3%–43.1%) [36–39].

Direct comparison between studies is not appropriate because of the different grading systems and diagnostic techniques used.

A strength of this study was the high response rate (88.1%). Despite the sophisticated equipment used in the examinations, people were not transported to a fixed examination site, but instead the examination site moved from cluster to cluster. A large, representative population-based sample was examined by SLB and retinal imaging. Another strength of the study is that the same experienced ophthalmologist (W. M.) was present throughout the study and examined all participants. However, a lack of stable electricity supply resulted in the number of people who had retinal images being reduced in some clusters.

A limitation of the study was our not having been able to obtain retinal images for all study participants. This is in large part due to the logistical constraints of performing electricity-dependent examinations in a setting where electricity supply cannot be guaranteed. Univariable analyses comparing those with gradable images ($n = 3,304$) and those without ($n = 83$) found significant differences. Those with no gradable images were more likely to be older, have poor vision, and have a cataract, thus the prevalence for this population may be slightly underestimated. The difference between the groups is likely due to a lack of stable electricity supply in the more rural clusters, where participants were demographically different.

When disease estimates using both methods were compared, SLB was found to have consistently under-diagnosed AMD. An analysis of the false negatives for late AMD revealed that lesions were noted but were not called neovascular AMD; instead they

Table 8. Visual acuity in those with AMD.

Visual Acuity	All AMD from Retinal Images	All AMD from SLB Only	Total AMD	No AMD	Total
Normal (≥6/12)					
Number	302	48	350	3362	3,712
Percent	75.1%	56.5%	71.9%	86.3%	84.7%
95% CI	(70.1–79.5)	(44.3–67.9)	(67.0–76.4)	(84.6–87.9)	(82.9–86.4)
Mild VI (<6/12–6/18)					
Number	23	16	39	185	224
Percent	5.7%	18.8%	8.0%	4.8%	5.1%
95% CI	(3.9–8.3)	(12.5–27.1)	(6.0–10.6)	(4.0–5.7)	(4.3–6.1)
Moderate VI (<6/18–6/60)					
Number	66	16	82	274	356
Percent	16.4%	18.8%	16.8%	7.0%	8.1%
95% CI	(12.7–21.0)	(11.9–28.5)	(13.4–20.9)	(6.2–8.0)	(7.2–9.2)
Severe VI (<6/60–3/60)					
Number	1	3	4	14	18
Percent	0.3%	3.5%	0.8%	0.4%	0.4%
95% CI	(0.03–1.2)	(1.2–9.8)	(0.3–2.2)	(0.2–6.4)	(0.3–0.7)
Blind (<3/60)					
Number	10	2	12	59	71
Percent	2.5%	2.4%	2.5%	1.5%	1.6%
95% CI	(1.2–5.0)	(0.6–9.2)	(1.3–4.8)	(1.2–2.0)	(1.2–2.1)
Total Number (Percent)	402 (100%)	85 (100%)	487 (100%)	3,894 (100%)	4,381 (100%)

VI, visual impairment.

doi:10.1371/journal.pmed.1001393.t008

were called macular scars. This may be a reflection of general practice in Africa, where it is often repeated in residency courses that "wet AMD" does not occur in Africans, as has been asserted in several studies [40,41]. This leads to late AMD being placed far down in the differential diagnosis for macular scars.

There was also discrepancy in identifying pigmentary lesions of early AMD. Retinal imaging identified many more hyperpigmented changes at the macula than did SLB. There are large natural variations in retinal pigmentation, resulting in colour differences between individuals. Such variation can tend to mask the more subtle variation between the important lesion types [42]. Studies have shown that the macular pigment density in other population groups is significantly lower than in African individuals [43]. The study ophthalmologist's perception of what constitutes increased pigment and what is normal background pigment in an African eye, in comparison to the reading centre's criteria, may have led to differences in classification.

Vision is measured based on the person's better eye, whereas AMD affects both eyes, and therefore a disparity between late AMD and poor vision can be seen. For example, there were 38 participants in the present study with late AMD, but only 16 with AMD and a visual acuity <6/60.

Disease subgroups included limited sample sizes, particularly for advanced AMD and blindness, which should be noted when interpreting the results.

Data collection began in 2007 and was based on electoral roll data from 2006. The population demographic is likely to have changed in the time to publication, and given population growth and increased survival, the estimated national prevalence of AMD could underestimate current prevalence.

Of note, location information collected from participants in this study will allow for incidence studies to be carried out in the future, thus providing new insights into the natural progression and incidence of AMD in this population.

Conclusion

Despite the long held belief that AMD is not a public health concern in Africa, this study provides evidence not only that is AMD as prevalent as in some other world regions (12.4% in this population), but also that it is an important problem contributing to both visual impairment and blindness in Africa. A total of 9.9% of blindness in this survey was attributable to AMD.

New therapeutic strategies have increased the available treatment options and improved prognostic perspectives for AMD in low-income countries [44]. However, these emerging treatments for AMD are largely unavailable in Kenya and most of Africa. When they become available, cost may be a major barrier towards accessing the treatment. Recent evidence suggests that bevacizumab is both effective and relatively affordable [45–47], but the infrastructure required to deliver an adequate AMD service, including the use of expensive optical coherence tomography machines, may be prohibitive. It is estimated that over 12 million people in Africa have low vision [48], and AMD is certainly a major contributor. Low vision services remain a hugely neglected area of care on the African continent; strengthening these services might be a cost-effective use of limited resources in the interim period. There is a need to train African-based ophthalmologists to improve recognition and treatment of AMD, particularly neovascular AMD, and a need for research to support the development of treatment programmes that are affordable and deliverable in Africa.

Supporting Information

Table S1 Comparison of those with diagnosis based on retinal images with those who had only SLB diagnosis.
(DOCX)

Table S2 Demographic characteristics including age as a continuous variable.
(DOCX)

Author Contributions

Conceived and designed the experiments: WM TP AF HK. Performed the experiments: WM. Enrolled patients: WM HK. Analyzed the data: WM AB AF HK. Wrote the first draft of the manuscript: AB WM. Contributed to the writing of the manuscript: AB WM HK TP AF. ICMJE criteria for authorship read and met: WM AB TP IL AF HK. Agree with manuscript results and conclusions: WM AB TP IL AF HK.

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Editors' Summary

Background. Worldwide, 39 million people are blind, and 246 million people (mainly living in developing countries) have moderate or severe visual impairment. The third leading global cause of blindness (after cataracts and glaucoma) is age-related macular degeneration (AMD). This group of conditions is characterized by lesions in the macular (central) region of the retina, the tissue at the back of the eye that converts light into electrical messages and sends them to the brain. AMD, which affects older people, destroys the sharp central vision that is needed for reading or driving, leaving only dim, blurred images or a black hole at the center of vision. AMD can be diagnosed by examining digital photographs of the retina or by examining the retina directly using a special magnifying lens (slit lamp biomicroscopy). There is no cure for AMD, although injections into the eye of certain drugs, such as bevacizumab, that block the activity of vascular endothelial growth factor can slow the rate of vision loss caused by some forms of AMD.

Why Was This Study Done? Most investigations of the prevalence (the proportion of a population with a disease) of AMD and of risk factors for AMD have studied people with European or Asian ancestry. Very little is known about AMD in African populations, and the data that are available mainly come from African populations living outside Africa. It is important to know whether AMD is an important cause of visual impairment and blindness in Africa, so that informed decisions can be made about the need for AMD programs in African countries. In this cross-sectional population-based study, the researchers investigate the prevalence of AMD among people aged 50 years or older living in Nakuru District (an ethnically diverse region of Kenya) and look for predictors of AMD in this population. In a cross-sectional population-based study, researchers observe a representative subset of a population at a single time point.

What Did the Researchers Do and Find? The researchers randomly selected 100 clusters of 50 people aged 50 years or older for their study. Between January 2007 and November 2008, study participants had a comprehensive eye examination and completed a standardized interview that included questions about their age, gender, other demographic details, medical history, and exposure to possible risk factors for AMD. Based on digital retinal images, the prevalences of early and late AMD among the study population were 11.2% and 1.2%, respectively. The prevalences of early and late AMD judged by slit lamp biomicroscopy were 6.7% and 0.7%, respectively. After controlling for age, women had a higher prevalence of both early and late AMD than men. The overall prevalence of AMD rose with age: compared to the youngest age group, the oldest age group had a three-fold higher risk of developing late AMD. Of the people with any grade of AMD, 25.6% had some visual impairment and 2.5% were blind. Overall, 9.9% of the blindness seen in the study was attributable to AMD.

What Do These Findings Mean? These findings identify AMD as an important cause of visual impairment and blindness in Nakuru District, Kenya. Extrapolation of these findings to the whole of Kenya suggests that 283,900 to 362,800 Kenyans had early AMD and 25,200 to 50,500 had late AMD in 2007. The accuracy of these findings is limited by the inability to obtain digital retinal images from all the participants (often because of electricity failures) and by other aspects of the study design. Moreover, because the methodology used in this study differed from some other studies of AMD, the prevalence of AMD reported here cannot be compared directly to those found in other studies. Nevertheless, these findings have several important implications. In particular, although recent evidence suggests that bevacizumab is likely to be both effective and affordable in Africa, the infrastructure required to deliver an adequate AMD service is currently prohibitively expensive in most African countries. Thus, these findings suggest that it is essential that research is undertaken to support the development of AMD treatment programs that are affordable and deliverable in Africa, and that low vision resources are provided for individuals with vision impairment.

Additional Information. Please access these websites via the online version of this summary at http://dx.doi.org/10.1371/journal.pmed.1001393.

- The US National Eye Institute provides detailed information about age-related macular degeneration
- The UK National Health Service Choices website also provides information about age-related macular degeneration, including personal stories about the condition
- The UK Royal National Institute of Blind People has information on age-related macular degeneration, including a video of a person describing their experiences of the condition
- AMD Alliance International provides written and audio information in several languages about age-related macular degeneration, including a large selection of personal stories; the Macular Degeneration Partnership also provides information about age-related macular degeneration, including a simulation of the condition
- MedlinePlus has links to additional resources about age-related macular degeneration (in English and Spanish)

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ORIGINAL PAPER

Prevalence and predictors of refractive error and spectacle coverage in Nakuru, Kenya: a cross-sectional, population-based study

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Abstract A cross-sectional study was undertaken in Nakuru, Kenya to assess the prevalence of refractive error and the spectacle coverage in a population aged ≥50 years. Of the 5,010 subjects who were eligible, 4,414 underwent examination (response rate 88.1 %). LogMAR visual acuity was assessed in all participants and refractive error was measured in both eyes using a Topcon auto refractor RM8800. Detailed interviews were undertaken and ownership of spectacles was assessed. Refractive error was responsible for 51.7 % of overall visual impairment (VI), 85.3 % ($n = 191$) of subjects with mild VI, 42.7 % ($n = 152$) of subjects with moderate VI, 16.7 % ($n = 3$) of subjects with severe VI and no cases of blindness. Myopia was more common than hyperopia affecting 59.5 % of those with refractive error compared to 27.4 % for hyperopia. High myopia (<−5.0 DS) was also more common than extreme hyperopia (>+5.0 DS). Of those who needed distance spectacles (spectacle coverage), 25.5 % owned spectacles. In conclusion, the oldest, most poor and least educated are most likely to have no spectacles and they should be specifically targeted when refractive services are put in place.

Keywords Refractive error · Spectacle coverage · Kenya · Visual impairment · Blindness

Introduction

Two hundred and eight-five million people worldwide are visually impaired with uncorrected refractive error (URE) being the leading cause worldwide, responsible

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for 42 % of all people with visual impairment including blindness [1]. URE is a priority of the World Health Organisation (WHO) and the International Agency for the Prevention of Blindness (IAPB) VISION2020 initiative [2]. The estimated global potential productivity loss was calculated at US dollars 121.4 billion in 2007 [3] and the correction of URE with spectacles has proven to be a cost-effective intervention in resource-poor settings [4].

The prevalence of blindness due to URE in sub-Saharan Africa (SSA) in the ≥50 age group was estimated by the WHO to be 1.64 % and the prevalence of VI was 5.94 % [5]. However, a recent review of URE in recent population-based studies in SSA [6] found the prevalence of URE blindness and URE VI in the same age group to be considerably lower. Six of 11 population-based studies reported no blindness due to URE. The proportion of moderate VI (presenting visual acuity [PVA] ≤6/60 and >6/18) due to URE ranged from 12.3 to 57.1 % [6].

The above review which included data from the Rapid Assessment of Avoidable Blindness (RAAB) study in the Nakuru district of Kenya demonstrated a prevalence of URE blindness of 0.09 % (95 % CI 0.06–0.10 %), with URE being responsible for 4.3 % of all persons found to be blind [7]. The RAAB methodology does not, however, quantify the levels or type of RE and further information is required to establish the prevalence of varying RE status amongst persons in Kenya, the spectacle coverage and the unmet need. We therefore undertook a population-based study in the same region as the previous RAAB study to provide local prevention of blindness programs with sufficient data to tackle this unmet need.

Methods

The study fieldwork was carried out in two phases from January 2007 to June 2007 and from April 2008 to November 2008. Detailed methodology has been described elsewhere [8], therefore relevant methods only are described here.

Sample size calculation

The sample size required was calculated based on an expected prevalence of VA < 6/12 in the better eye of 3.0 % among those aged ≥50 years, a required precision of 0.5 % (95 % CI), a design effect of 1.5, and a response rate of 90 %, so that 4,996 participants were needed (Epi Info 6.04, Centers for Disease Control and Prevention, Atlanta, GA, USA). We therefore aimed to select 100 clusters with each containing 50 participants.

Sampling strategy and recruitment

As recent census data for Kenya were not available [9], election role lists that were renewed in 2006 in preparation for the 2007 general elections were used as the sampling frame for this survey. The population size was updated for the year 2007 using a population growth rate of 2.7 % per year [10]. One hundred clusters were selected with a probability proportional to the size of the population. A cluster was defined as the area served by the polling station.

Households were selected within clusters using a modified compact segment sampling method [11]. An eligible individual was defined as someone aged ≥50 years living in the household for at least 3 months in the previous year. Age was determined using the subject's testimony, national identity cards and a calendar of historic events.

Ophthalmic and general examination

Suitable predetermined examination sites were selected on the recommendation of the village leader with close proximity for access to the cluster and electricity supply (mains or generator) for the equipment.

Visual acuity

The presenting distance VA was defined as the number of letters read correctly without glasses if the participant did not have glasses or with their own glasses if they were present. Testing was carried out on each eye separately at 4 meters using a reduced LogMAR tumbling 'E' chart [12] in a well-lighted area. If the subject's vision was too poor to read any letters on the chart at four meters, then the subject was tested at 1 meter, then as follows:

- Counting fingers (CF)—ability to count fingers at 1, 2 or 3 meter distance.
- Hand motion (HM)—ability to distinguish if a hand is moving or not in front of the patient's face.

- Light perception (LP)—ability to perceive any light.
- No light perception (NLP)—inability to see any light or total blindness.

Those who did not read 24 letters (VA < 6/12) at 4 meters were scheduled for correction and to undergo a repeat VA measurement with the correction in place.

Presenting near VA, was assessed in daylight, binocularly using a continuous chart with N8, N10, N14 and N24 type held a constant 40 cm from the participant's face.

Refractive error

Presenting VA (aided or unaided) was measured on all participants. Participants with presenting unaided distance vision ≥6/12 Snellen equivalent in the better eye were deemed not to have vision-impairing RE and did not require RE correction. Participants with presenting uncorrected distance vision <6/12 in the better eye who improved to ≥6/12 with pinhole were defined as having VI caused by RE requiring correction. If there was no improvement to 6/12 with pinhole and no other pathology was present to explain the vision loss, their VI was attributed to other than pathology. Such participants were referred for treatment for the cause attributed to the VI and were declared not to require RE or presbyopia correction.

If a participant presented with distance spectacles that provided vision ≥6/12 in the better eye they were deemed to have a visually significant RE that was satisfactorily corrected with their current correction. When the presenting corrected distance vision was <6/12 in the better eye, but improved to at least 6/12 with pinhole, an under-corrected RE was determined to be present and they were deemed to need further correction and replacement spectacles.

An automated Topcon auto refractor RM8800 was used to provide an objective non-cycloplegic measurement of all participants who needed RE correction for distance. Measurement of the sphere −25 D to +22 D (to the nearest 0.25 D), cylinder 0 D to ±10 D (to the nearest 0.25 D) and axis 0° to 180° (in 5° steps) were recorded. Each patient who did not see ≥6/12 with RE needing correction as defined above was corrected using the auto refractor correction and VA retested to confirm improvement to ≥6/12. Subjective refraction correction was only carried out if the auto refractor correction did not result in VA ≥6/12. The corrections used for the study were not considered as the final prescription. Instead all participants with RE were referred for final prescriptions at the district hospital.

Near vision

Participants in this study, all of whom were aged ≥50 years, were considered to have presbyopia if they could see binocular N8 with their presenting near spectacles, or if they were unable to read N8 with (under-corrected) or without (uncorrected) presenting near spectacles as long as they had normal distance vision or their pinhole distance vision was ≥6/12. Participants who had pinhole distance vision worse than 6/12 in the better eye and did not see binocular N8 were not included in the presbyopia group.

Presbyopia correction was defined as the smallest of five corrections (+1.0, +1.5, +2.0, +2.5, +3.0) that allowed the participant to see N8.

General information

Detailed interviews were undertaken in the local language covering demographic details, information on risk factors, socio-economic status and full past medical history. We also measured weight, height, waist and hip circumference, blood pressure, and random cholesterol and glucose blood levels [13].

Data entry

A data entry package in EpiData Entry v 2.1 was developed for this study, which incorporated range and consistency checks. Data was entered by two data entry clerks on separate computers. Consistency checks were performed each evening and inconsistencies corrected on the same day. Two datasets, one for the demographic and risk factor information and one for the ophthalmic examinations, were stored each bearing the same study identification.

Definitions used

RE was presented as spherical equivalent, taken as the sphere power plus half the cylinder power. Statistical analysis was performed on data from right eyes only in keeping with methodology used in similar studies

[14], as the correlation between the spherical equivalent in the right and left eye was acceptable (Pearson's coefficient 0.57) with no significant differences between the right and left eyes on paired t test ($p = 0.19$). The following definitions were used at analyses stage:

- Refractive status refers to the refractive status on auto refraction irrespective of Topcon auto refractor RM8800y. No cycloplegic refraction was performed.
- RE in this study is defined as a presenting vision <6/12 in the better eye which improves to ≥6/12 after correction.
- Spherical RE was presented as the spherical equivalent, which equals the sphere power plus half the cylinder power.
- Myopia was defined as the spherical equivalent of −0.5 D or less. The myopia was categorized as mild myopia (−0.5 D to −3.0 D), moderate myopia (−3.1 D to −5.0 D) or high myopia (less than −5.0 D). Clinically significant myopia was defined as a spherical equivalent myopia of at least −1.0 D.
- Hyperopia was defined as the spherical equivalent of more than +0.5 D. Hyperopia was categorized as low hyperopia (+0.5 D to +3.0 D) and high (>+3.1 D). Clinically significant hypermetropia was defined as a spherical equivalent hyperopia of at least +3.0 D.
- Emmetropia was defined as the spherical equivalent of between +0.5 D and −0.5 D.
- Astigmatism was defined as >0.5 D of minus cylinder, without reference to the axis. Astigmatism was measured in negative cylinders with the axis of astigmatism defined as with the rule (0° ± 15°), against the rule (90° ± 15°), or oblique (16–74° and 106–164°).
- Anisometropia was defined as a difference in the spherical equivalent between the right and left eyes of >1.0 D. Data for those with no left eye information was not included in the analyses as well as for those who had cataract surgery in the left eye.
- 'Off the shelf' implies a refractive range that can be corrected with ready-made glasses.

Ethical approval

Ethical approval was granted by the LSHTM Ethics Committee and also the Kenya Medical Research Institute. Approval was also granted by the Provincial Medical Officer Rift Valley and the Nakuru district Medical Officer of Health. Written approval was sought from the administrative heads in each cluster, usually the village chief. All participants gave witnessed written or verbal consent to participate. People requiring medical treatments were referred to the appropriate center.

Data analysis

Prevalence of RE strata, URE blindness and VI was estimated, and the cluster design effect (DEFF = 1.5) of the study was taken into account when calculating confidence intervals surrounding the prevalence estimates.

Socio-economic status: a continuous asset score was produced using a scoring system derived through principal component analysis in an earlier study in this setting [15, 16]. The score was divided into quartiles to categorize the study participants into four socioeconomic groups with a higher score representing higher SES.

Obesity using waist circumference was categorized using WHO guidelines [17] as normal (male <94 cm, female <80 cm), overweight (male 94–101.9 cm, female 80–87.9 cm) and obese (male ≥102 cm, female ≥88 cm).

The clusters were defined as rural or urban according to the classification used by the District Health Statistics office [18]. The distinctions were made nationally based on population density, administrative function, availability of social amenities and physical infrastructure such as hospitals, post office, schools, and markets.

Results

Study participation and response rates

Of the 5,010 subjects eligible for this study, 4,414 underwent examination (response rate 88.1 %). The response rate was similarly high among men (89.2 %) and women (86.5 %). Of the non-respondents, 584 (98 %) were away working or visiting family outside the cluster location, and 12 (2 %) refused to participate.

Comparison of responders and non-responders

Details about gender were available for all of the non-responders while age was available for 526 non-

responders (90.1 %). Those who were examined were significantly older (mean age 63.4 years, SD 10.5 years) than those who were not (61.9, SD 10.6 years, $p = 0.002$). Women were significantly over-represented among the non-responders (56.8 %) compared to those who were examined (52.1 %, $p = 0.03$). Of those eligible, 66.5 % were from rural clusters while 67.2 % of those who were examined were from rural areas ($p = 0.7$). Of those who were not examined none were believed to be blind.

Analysis

Among those who responded 33 had incomplete examinations, or missing data. Therefore 4,381 participants were included in the ophthalmic analyses.

Of the 4,381 participants with complete data, 669 had visual impairment and 71 of these were blind.

RE was responsible for 51.7 % of overall VI (i.e., those with VA <6/12), 85.3 % ($n = 191$) of subjects with mild VI, 42.7 % ($n = 152$) of subjects with moderate VI, 16.7 % ($n = 3$) of subjects with severe VI and no cases of blindness.

There were 346 individuals whose main cause of VI was RE, i.e., VA <6/12 Snellen equivalent that improved to ≥6/12 on correction. Ten individuals whose cause of VI was determined to be aphakia were excluded from the analysis but were included in the analyses for spectacle coverage.

Comparison of PVA and best-corrected visual acuity showed that most (69.0 %) of the participants who were categorized as blind based on PVA could not be improved by correcting their refraction status whereas the majority of those with severe VI (66.7 %) or moderate VI (63.8 %) could be improved at least one category (Table 1). Of those with mild VI, 86.7 % improved on refraction to normal VA. Of the 22 participants who improved from blind to severe VI on correction, nine had dense nuclear sclerotic cataract, five were aphakic or had experienced surgical complications while the rest had retinal pathology (two with glaucoma, three with other retinopathies, and three with age-related macular degeneration). Three hundred and fifty-six people with some level of VI on PVA, representing 8.1 % of participants, improved to normal vision on correction (Table 2).

Types of RE

Myopia was much more common than hyperopia affecting 59.5 % of those with RE compared to 27.4 % for hyperopia. High myopia (<−5.0 DS) was also more common than extreme hyperopia (>+5.0 DS).

Men had significantly more myopia than women ($p = 0.05$) while women had significantly more hyperopia than men ($p = 0.0001$; OR 2.5; 95 % CI 1.5–4.2). Of the 45 people with emmetropic results, 13 had moderate VI and 32 had mild VI. The 13 patients with moderate VI as well as 25 of the others had significant astigmatism (>0.5 Dcyl). Overall the prevalence of RE in the study was 7.4 % and the difference in prevalence between men and women was not significant ($p = 0.31$).

Suitability for ready-made (off the shelf) distance spectacles

Eighty-one people with hypermetropia, 113 people with myopia and 45 people with near emmetropic (−0.5 to +0.5 DS equivalent [excluding plano]) refraction were within the range of 'off the shelf'

Table 1 Comparison of presenting VA and best-corrected VA

		Best-corrected visual acuity					
		Normal	Mild VI	Moderate VI	Severe VI	Blind	Total
Presenting visual acuity	Normal	3,712 (100 %)					3,712 (100 %)
	Mild VI	194 (86.7 %)	30 (13.4 %)				224 (100 %)
	Moderate VI	157 (44.1 %)	70 (19.7 %)	129 (36.2 %)			356 (100 %)
	Severe VI	3 (16.7 %)	2 (11.1 %)	7 (38.9 %)	6 (33.3 %)		18 (100 %)
	Blind	2 (2.8 %)	0	17 (23.9 %)	3 (4.2 %)	49 (69.0 %)	71 (100 %)
	Total No.	4,068	102	153	9	49	4,381

VI visual impairment

Table 2 Distribution of RE results presented as spherical equivalent for those whose principal cause of VI is RE

Range	Males *n* (%)	Females *n* (%)	Total *n* (%)
>+5.01 high hypermetropia	6 (3.4 %)	2 (1.2 %)	8 (2.3 %)
+3.01 to +5.00 DS	0	5 (3.0 %)	5 (1.5 %)
+0.51 to +3.00 DS off the shelf[a]	23 (13.0 %)	58 (34.9 %)	81 (23.6 %)
Total hyperopia	29 (16.4 %)	65 (39.2 %)	94 (27.4 %)
−0.50 to +0.50 DS off the shelf[a] excluding plano	25 (14.1 %)	20 (12.1 %)	45 (13.1 %)
−0.51 to −3.00 DS off the shelf[a]	68 (38.4 %)	45 (27.1 %)	113 (32.9 %)
−3.01 to −5.0 DS	37 (20.9 %)	18 (10.8 %)	55 (16.0 %)
<−5.01DS high myopia	18 (10.2 %)	18 (10.8 %)	36 (10.5 %)
Total myopia	123 (69.5 %)	81 (48.8 %)	204 (59.5 %)
Total with RE	177 (100 %)	166 (100 %)	343 (100 %)
Prevalence of RE in study	7.8 % (95 % CI 6.6–9.2)	7.0 % (95 % CI 5.8–8.3)	7.4 % (95 % CI 6.5–8.4)

DS dioptre sphere, *RE* refractive error, *CI* confidence interval

[a] 'Off the shelf' implies a refractive range that can be corrected with ready-made glasses

spectacles using spherical equivalents (total 239 people). However 207 of them had significant astigmatism (>0.5 Dcyl) or anisometropia (>1.0 D difference between eyes) leaving only 32 (9.3 %) suitable for 'off the shelf' spectacles.

Distance vision spectacle coverage

Of the 4,381 subjects examined, 69 men and 53 women had distance spectacles. However, another 346 subjects with RE and 10 subjects with aphakia could have had their presenting vision improved to ≥6/12 if they wore spectacles. Coverage for distance spectacles was therefore only 25.5 % and there was no significant difference between men (27.2 %) and women (23.7 %) in coverage (Pearson χ^2 (1) = 0.77 Pr = 0.38) as shown in Table 2.

Predictors of having distance spectacles

Univariate and multivariate analysis was performed with logistical regression of key variables with RE including age, gender, literacy, education, occupation, and residence (urban or rural) to predict spectacle usage (Supplementary Table 1). Univariate analyses revealed that the older people were then the less likely they were to wear glasses. Women were also less likely to wear spectacles than men. Those who were less poor, better educated, living in urban areas or diabetics were more likely to have distance spectacles when they needed them. After multivariate analyses, the same factors remained significantly associated with the unmet need for distance spectacles.

Presbyopia

Among those with best-corrected VA ≥ 6/12, 3,993 patients were tested for presbyopia. Among them, 3,686 had presbyopia giving a prevalence of 92.3 % (95 % CI 90.4–93.9). The prevalence in men and women was equal at 92.3 % ($p = 0.99$) as was the difference between rural and urban dwellers (91.7 vs 93.6 %, respectively $p = 0.3$).

Only 400 of those with presbyopia (10.9 %) presented with reading glasses that allowed them to see N8.

Table 3 Spectacle coverage in men and women

	Male	Female	Total
Met need (wears distance spectacles and achieves ≥6/12 in the better eye)	69 (27.2 %)	53 (23.7 %)	122 (25.5 %)
Unmet need (needs distance spectacles to achieve ≥6/12 in the better eye)	185 (72.8 %)	171 (76.3 %)	356 (74.5 %)
Total need	254 (100 %)	224 (100 %)	478 (100 %)
Coverage (met need/total need)	27.2 %	23.7 %	25.5 %

Discussion

Unlike studies in similar elderly populations in Europe, Australia, Latin America and Asia [19–23], RE did not cause any blindness in this study. The recent Nigeria National Survey of Blindness [24] found 1.4 % of blindness was caused by RE suggesting low levels even in West Africa. However, in this survey as in Nigeria, RE was the leading cause of mild and moderate VI. In contrast, the Tema Survey, a population-based survey in Ghana found a high prevalence of RE-related blindness and VI [25]. Major genetic variations between people of West and East African origin have been described which may account for the differences between the two populations. The Tema Survey also examined a younger age group, including participants aged ≥40 years. The 40–49 year age group was not included in the Nakuru Survey; however, this age group in the Ghanaian study included the greatest number of participants and, as expected, age-related causes of VI such as cataract were low in this group.

The widely used RAAB methodology had also been previously implemented in this population [7]. RE in the RAAB study was responsible for 4.3 % of blindness, 7.4 % of severe VI and 31.5 % of moderate VI. This overestimated the level of blindness due to RE compared to the more accurate measures of RE and underestimated levels of VI due to RE. Although pinhole assessment used in the RAAB study is a useful and rapid screening test for RE, it is unable to exclude vision loss due to other pathologies or quantify levels or type of RE.

Correction of RE is a cost-effective implementation and can significantly improve both quality of life and ability to function in society.

In the age group studied, presbyopia is highly prevalent and has an impact on the ability to carry out near-vision-related tasks. The prevalence of presbyopia in this study (92.3 %) was similar to that found in a smaller study in the same population [26] which looked at functional presbyopia in which 130 eligible participants were selected for near-vision testing and interview. Functional presbyopia was found in 85.4 % ($n = 111$) [26].

It is also similar to a study in Zanzibar that found an overall prevalence of presbyopia of 89.2 % [27, 28]. Among those with presbyopia in this study only 10.9 % had spectacles compared to 17.6 % in Zanzibar but equal to the presbyopia coverage in the same age group in another East African population in Tanzania [29]. Cost was cited as the main barrier to spectacle use in 62 % of participants with presbyopia in the earlier smaller study in this population [26].

Among participants with functional presbyopia, 5.4 % wore reading glasses and 25.2 % had prior contact with an eye care professional. The unmet presbyopic need was 80.0 %, the met presbyopic need was 5.4 % and presbyopic correction coverage was 6.3 %. Cost was cited as the main barrier to spectacle use in 62 % of participants with presbyopia [26].

Provision of optical services in Africa has remained largely in the hands of the private sector making spectacles usually unaffordable for the vast majority of those who need them. Several more complex barriers to spectacle provision and wear exist [30]; however, affordability and availability remains a major obstacle. This explains the low spectacle coverage in this study in an elderly population where public provision of refractive services and low-cost spectacles is non-existent. A large number of private optometrists are situated in Nakuru town; however, these services are heavily reliant on auto refractors for providing final prescriptions and the cost of spectacles is too high for those most in need.

Based on up-to-date census data we estimate that between 250,000 and 320,000 adults >50 years of age in Kenya are visually impaired due to RE, of whom currently only approximately one-quarter are wearing adequate correction.

The oldest, most poor and least educated are most likely to have no spectacles and they should be specifically targeted when refractive services are put in place.

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